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Clinical Medicine

Kerry Layne

Series Editor: Janice Rymer



100 Diagnostic Dilemmas in Clinical Medicine



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100 Diagnostic Dilemmas in Clinical Medicine

Dr Kerry Layne MBBS BSc (HONS) MRCP

Specialist Registrar in Clinical Pharmacology and
Therapeutics/General Medicine, Guy's & St Thomas'
NHS Foundation Trust, London, UK

100 Cases Series Editor:

Janice Rymer

Professor of Obstetrics & Gynaecology and Dean of Student Affairs,
King's College London School of Medicine, London, UK



CRC Press

Taylor & Francis Group
Boca Raton London New York

CRC Press is an imprint of the
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CRC Press
Taylor & Francis Group
6000 Broken Sound Parkway NW, Suite 300
Boca Raton, FL 33487-2742

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Printed on acid-free paper

International Standard Book Number-13: 978-1-138-72094-7 (Hardback)

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Library of Congress Cataloging-in-Publication Data

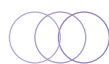
Names: Layne, Kerry, author.
Title: 100 diagnostic dilemmas in clinical medicine / Kerry Anne Layne.
Other titles: One hundred diagnostic dilemmas in clinical medicine
Description: Boca Raton : CRC Press/Taylor & Francis Group, [2017] | Includes bibliographical references and index.
Identifiers: LCCN 2017003164 (print) | LCCN 2017004018 (ebook) | ISBN 9781498728522 (pbk. : alk. paper) | ISBN 9781138720947 (Hardback) | ISBN 9781482238174 (Paperback) | ISBN 9781482238181 (E-Book)
Subjects: | MESH: Clinical Medicine | Diagnosis, Differential | Case Reports
Classification: LCC RC71.5 (print) | LCC RC71.5 (ebook) | NLM WB 293 | DDC 616.07/5--dc23
LC record available at <https://lccn.loc.gov/2017003164>

Visit the Taylor & Francis Web site at
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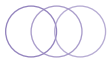
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PREFACE

Over recent years, case-based learning has become increasingly acknowledged as a valuable teaching method that encourages recognition of particular clinical presentations and enables the learners to place themselves in the role of the decision maker. The scenarios in this book are loosely based on cases that a large group of doctors has encountered over their careers, and which they have subsequently found invaluable when teaching their peers and their students. Each case provides a unique diagnostic challenge, as indeed do so many of the patients that doctors encounter in daily clinical practice. We hope they will stimulate your interest in clinical medicine and guide you when caring for your future patients irrespective of the symptoms with which they present.

Kerry Layne
London
November 2016



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ACKNOWLEDGEMENTS

With many thanks to Dr Boris Lams, Dr Mark Kinirons, Dr Stephen Thomas, Dr Anne Collett, Dr Anna Goodman, Dr Rex Muza and Prof. Cathy Nelson-Piercy, who have all given up so many early mornings to promote case-based learning. Their expertise and passion for teaching has been invaluable.



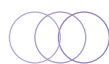
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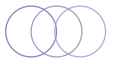
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ABBREVIATIONS

ABG	Arterial blood gas
ACTH	Adrenocorticotrophic hormone
AFB	Acid-fast bacilli
Alb	Albumin
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
AMTS	Abbreviated mental test score
ANA	Anti-nuclear antibody
ANCA	Anti-neutrophil cytoplasmic antibody
APLS	Antiphospholipid
AST	Aspartate aminotransferase
ATP	Adenosine triphosphate
BD	Twice daily
BE	Base excess
β-HCG	Beta-subunit of human chorionic gonadotrophin (pregnancy test)
Bili	Bilirubin
BMI	Body mass index
BP	Blood pressure
bpm	Beats per minute
cCa	Corrected calcium level
CK	Creatine kinase
CMV	Cytomegalovirus
CNS	Central nervous system
CO ₂	Carbon dioxide
COPD	Chronic obstructive pulmonary disease
Creat	Creatinine
CRP	C-reactive protein
CSF	Cerebrospinal fluid
CT	Computed tomography
CTPA	CT pulmonary angiogram
DBP	Diastolic blood pressure
DIC	Idiopathic thrombocytopenic purpura
DNA	Deoxyribonucleic acid
DVT	Deep vein thrombosis
E°	Eosinophil count
EBV	Epstein–Barr virus
ECG	Electrocardiogram
EEG	Electroencephalogram
EGPA	Eosinophilic granulomatosis with polyangiitis
ENA	Extractable nuclear antigen antibody
ENT	Ear, nose and throat



ESR	Erythrocyte sedimentation rate
FFP	Fresh frozen plasma
g	Gram
GABA	γ -Aminobutyric acid
GBM	Glomerular basement membrane
GCS	Glasgow Coma Scale
GGT	Gamma glutamyl transferase
GP	General practitioner
Hb	Haemoglobin
HbA1c	Glycated haemoglobin
HCO ₃	Bicarbonate
HDL	High-density lipoprotein
HIV	Human immunodeficiency virus
HR	Heart rate
HSV	Herpes simplex virus
IBD	Inflammatory bowel disease
ICP	Intracranial pressure
IgA	Immunoglobulin A
IgE	Immunoglobulin E
IgG	Immunoglobulin G
IgM	Immunoglobulin M
INR	International normalised ratio
IRIS	Immune reconstitution inflammatory syndrome
ITP	Idiopathic thrombocytopenic purpura
IV	Intravenous
IVIg	intravenous immunoglobulin
JVP	Jugular venous pressure
K	Potassium
L	Litre
L ^o	Lymphocyte count
LDL	Low-density lipoprotein
LFT	Liver function test
MAHA	Microangiopathic haemolytic anaemia
MCV	Mean corpuscular volume
mg	Milligram
Mg	Magnesium
mL	Millilitre
mm	Millimetre
MMR	Measles, mumps and rubella
MR	Magnetic resonance
MRA	Magnetic resonance angiography
MRCP	Magnetic resonance cholangiopancreatography
MRI	Magnetic resonance imaging
MSU	Mid-stream urine collection (for culture)



N°	Neutrophil count
Na	Sodium
NMDA	<i>N</i> -methyl-D-aspartate
NPH	Normal pressure hydrocephalus
NSAID	Non-steroidal anti-inflammatory drug
NT pro-BNP	Brain natriuretic protein
O ₂	Oxygen
OD	Once daily
OGD	Oesophago-gastro-duodenoscopy
ON	Once at night
PAN	Polyarteritis nodosa
pCO ₂	Partial pressure of carbon dioxide
PCP	<i>Pneumocystis jirovecii</i> pneumonia
PCR	Polymerase chain reaction
PE	Pulmonary embolism
PET	Positron emission tomography
PFO	Patent foramen ovale
Plt	Platelet count
PO	Oral
pO ₂	Partial pressure of oxygen
PO ₄	Phosphate
QDS	Four times daily
RNA	Ribonucleic acid
RPR	Rapid plasma reagin
RR	Respiratory rate
RRT	Renal replacement therapy
SBP	Systolic blood pressure
SLE	Systemic lupus erythematosus
SpO ₂	Peripheral capillary oxygen saturation ('sats')
STI	Sexually transmitted infection
T	Temperature
TB	Tuberculosis
TDS	Three times daily
TnT	Troponin T
TTP	Thrombotic thrombocytopenic purpura
UPSI	Unprotected sexual intercourse
VBG	Venous blood gas
V/Q	Ventilation/perfusion
VZV	Varicella-zoster virus
WCC	White cell count



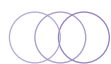
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REFERENCE RANGES FOR COMMON INVESTIGATIONS

	Reference range	Units
Full blood count		
White cell count	4.0–11.0	×10 ⁹ /L
Neutrophil count	2.0–7.0	×10 ⁹ /L
Lymphocyte count	1.0–4.0	×10 ⁹ /L
Eosinophil count	0.1–0.4	×10 ⁹ /L
Haemoglobin level	120–160	g/L
Platelet count	150–400	×10 ⁹ /L
Mean corpuscular volume	80–100	fL
Renal profile		
Sodium	135–145	mmol/L
Potassium	3.5–5.0	mmol/L
Urea	2.5–7.8	mmol/L
Creatinine	60–100	µmol/L
Liver function tests		
Bilirubin	05–21	µmol/L
Alanine aminotransferase	05–40	IU/L
Alkaline phosphatase	30–130	IU/L
Gamma glutamyl transferase	7–40	IU/L
Albumin	35–50	g/L
Additional electrolytes		
Corrected calcium	2.20–2.60	mmol/L
Phosphate	0.8–1.3	mmol/L
Magnesium	0.75–1.2	mmol/L
Endocrine tests		
Thyrotropin (thyroid-stimulating hormone)	0.2–5.0	mIU/L
Plasma glucose level	4.0–8.0	mmol/L
HbA1c level	20–42 (4.0–5.9)	mmol/mol (%)
Amylase	<90	IU/L
Inflammatory biomarkers		
C-reactive protein	<1	mg/L
Erythrocyte sedimentation rate	0–22	mm/hr
Coagulation tests		
INR	0.8–1.2	
D-dimer	<0.45	µgFEU/mL
Cardiac tests		
NT pro-BNP	<300	ng/L
Troponin T	<14	ng/L
(Continued)		



	Reference range	Units
Arterial blood gas		
pH	7.35–7.45	
pO ₂	10.5–13.5	kPA
pCO ₂	4.7–6.0	kPA
Bicarbonate	22–26	mEq/L
Base excess	–2 to +2	mmol/L
Lactate	0.5–1.0	mmol/L

CASE 1: A TEENAGER WITH RASH AND A FEVER

PATIENT HISTORY

A 17-year-old woman presented to hospital complaining of a rash and profound lethargy. The rash initially began over her face and neck and then spread to involve her trunk. For the preceding 5 days, she had been experiencing coryzal symptoms, headaches, fevers and joint pains. Her medical history included childhood asthma. She took no regular medications and had no known drug allergies. She lived with her mother and had one regular sexual partner. She worked as a receptionist and did not smoke or drink alcohol. She had not travelled abroad for more than 5 years. The patient's friends, family and colleagues were not known to be unwell.

EXAMINATION

Initial observations: 36.1°C, HR 67 bpm, BP 113/65 mm Hg, RR 22, SpO₂ 99% on room air.

The patient was alert and orientated. Her mucous membranes were dry. She had a violaceous rash covering her face and trunk (see [Figure 1.1](#)). The rash was erythematous, maculopapular and blanching. The lesions were tender to touch and, although they were generally discrete, some appeared confluent. The patient was coughing frequently, but her chest sounded clear. Cardiovascular and abdominal assessments were unremarkable. Her neck muscles were tender (although she had full range of movement), and she was photophobic. There was mild, generalised abdominal tenderness and widespread arthralgia. There was no lymphadenopathy. There was no conjunctival injection.

INITIAL RESULTS

Routine bloods: WCC 5.0, Hb 140, Plt 187, Na 138, K 3.9, Creat 54, CRP 24.



Figure 1.1 The image shows an erythematous, maculopapular facial rash.



DIFFERENTIAL DIAGNOSES

A history of fevers, coryzal symptoms and a rash makes a viral exanthem the most likely diagnosis. Causes of viral exanthemata include rubella, parvovirus B19 and measles, as well as more common viruses, such as rhinovirus. A history of travel would lead to a wider differential of viruses present outside of the United Kingdom. The rash and history of fever and non-specific viral symptoms could represent a seroconversion illness and an HIV test should be offered.

A fixed drug eruption could cause this constellation of symptoms if she happened to have a co-incident coryzal infection with rhinovirus, for example. The patient should be asked whether she has taken any new medications recently, particularly antibiotics, anticonvulsants or non-steroidal anti-inflammatory drugs (NSAIDs).

Other less likely diagnoses include infectious mononucleosis (due to HIV, toxoplasmosis, cytomegalovirus [CMV] or Epstein–Barr virus [EBV]), but lymphadenopathy would be expected and was not present. Although she has only one sexual partner, we cannot be sure of the partner's history so a sexually transmitted infection (STI) screen is essential to rule out syphilis. A history of cough, fever and generalised rash might suggest *Mycoplasma pneumoniae* infection. Toxic shock syndrome should also be considered as, although this is unlikely, it is potentially serious.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient should be isolated immediately. The history should be reviewed, in particular focusing on her childhood illnesses and vaccinations, medication history, travel history, recent use of menstrual tampons (associated with toxic shock syndrome) and a history of insect bites or wounds. Her mucous membranes appear dry, but she is haemodynamically stable with a normal renal profile. She should be encouraged to drink water rather than commencing intravenous rehydration at present. A chest x-ray should be performed to look for areas of consolidation, indicative of infection. Antibiotics are not indicated currently.

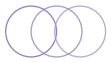
In view of the fever, blood and urine samples should be sent for culture. A salivary swab should be sent for measles testing and serology for parvovirus, rubella and mycoplasma in addition to HIV, syphilis, CMV and EBV if there is clinical suspicion.

As there are signs of meningism, a lumbar puncture is indicated.

CASE PROGRESSION

The patient was seen by the medical team who noted a tonsillar exudate and lesions around the oral mucosa, extending to the palate. Both knee joints appeared swollen with small effusions. She was admitted to an isolated room and a full septic screen was performed. Due to poor oral intake, intravenous fluid rehydration was commenced. No antibiotic or antiviral agents were commenced. There were no signs of meningism by this stage and a lumbar puncture was therefore not performed. A ferritin level was sent as a potential marker for adult Still's disease. An autoimmune profile was also requested.

The infectious diseases team reviewed the patient the following day. They advised sending viral serology tests and swabs of the oral mucosa lesions. A monospot test and anti-streptolysin O titre were taken.



The patient improved after 48 hours of conservative management and her symptoms resolved. She was discharged home at this stage. She was followed up in the outpatient infectious diseases clinic where the remainder of her investigations were reviewed. Her mouth swabs were positive for measles RNA. Measles IgM and IgG tests were positive.

Final diagnosis: Primary measles infection.

OUTCOME

The patient made a full recovery. Further history taking established that she had not received measles/mumps/rubella (MMR) vaccinations due to parental concerns regarding data that had falsely linked MMR vaccination and the development of autism. She received the MMR vaccination 2 months after her illness.

CASE DISCUSSION

Measles typically presents with a high fever followed by a prodrome of influenza-like symptoms with conjunctivitis, and later, a blanching, erythematous maculopapular rash. Koplik spots may be visible around the buccal mucosa in the early stages of the infection.

In this case, viral mouth swabs were positive for measles RNA – this is the gold standard test for identifying measles infection. Both her measles IgG and IgM tests were positive – these blood tests were taken at a relatively late stage of her illness and this is therefore in keeping with a primary measles infection.

The treatment of measles is largely supportive, with fluids and analgesia. Complications can include pneumonia, meningitis and acute disseminated encephalomyelitis. Vitamin A plays an essential role in immune modulation and supplementation should be given in patients with measles who are at risk of vitamin A deficiency.

Two doses of a measles-containing vaccine are required to protect against measles infection. Measles is becoming increasingly common in young adults, predominantly due to a reduction in MMR vaccine uptake following the aforementioned data publication. This patient received both doses of the MMR vaccination once she had recovered.

In the United Kingdom, measles is a notifiable illness and the Health Protection Agency should be informed when a confirmed measles case occurs to allow contact tracing where appropriate. In this case, the patient had no siblings and all close contacts remained well.

With thanks to Dr Jon Lambourne and Dr Henry Fok for their help with this case.

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CASE 2: HEPATITIS IN A NIGHTSHIFT WORKER

PATIENT HISTORY

A 28-year-old man presented to hospital complaining of abdominal pain and yellow sclera. He described a 3-week history of right upper quadrant pain that was exacerbated by eating. The pain was dull in nature and did not radiate. He had noticed his sclera becoming yellow over the preceding 3–4 days. On direct questioning, he admitted to dark urine and pale stools. He denied weight loss, fevers and night sweats. He had no past medical history and took no regular medications, although he had occasionally been using paracetamol to treat his abdominal pain. He was of Somali origin and had last travelled to Somalia 6 months earlier. He was in a monogamous relationship and worked nightshifts as a security officer. He smoked 20 cigarettes daily but did not drink alcohol.

EXAMINATION

Initial observations: T 36°C, HR 80 bpm, BP 128/80 mm Hg, RR 16, SpO₂ 97% on room air.

The patient was alert and orientated. He appeared markedly icteric. Abdominal examination revealed right upper quadrant tenderness and a 1 cm palpable liver edge. There were no additional stigmata of liver disease. Cardiovascular and respiratory examinations were unremarkable.

INITIAL RESULTS

Routine bloods: WCC 6.2, Hb 152, Plt 230, Na 137, K 3.8, Creat 57, Bili 101, ALT 1318, ALP 199, GGT 171, INR 1.1, Amylase 57.

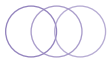
DIFFERENTIAL DIAGNOSES

The deranged liver function tests represent a hepatic picture and all causes of an acute hepatitis should be considered.

Viral infections such as hepatitis A, B, C and E should be tested for. Blood tests should also be sent to test for cytomegalovirus (CMV) and Epstein–Barr virus (EBV). An HIV test should be performed – patients with hepatitis B and C infection are more likely to have established HIV co-infection.

Autoantibodies, including anti-nuclear antibodies (ANA) and anti-smooth muscle antibodies may be useful in the diagnosis of autoimmune hepatitis, although histological examination following a liver biopsy is the gold standard test.

A thorough drug history may elicit the cause of hepatitis. The patient has reported paracetamol use over the preceding week and a potential paracetamol overdose may have occurred. Both



medicinal and recreational drug histories should be fully established and management of paracetamol overdose may need to be initiated.

Alcohol remains one of the more common causes of acute hepatitis. Alcoholic hepatitis is a clinical diagnosis, but a history of high alcohol intake and negative viral and autoimmune tests will support the diagnosis. A high AST:ALT ratio (>2) is suggestive of excessive alcohol intake.

Rarer causes, such as haemochromatosis and Wilson's disease, can be considered where appropriate.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

You need to establish how much paracetamol the patient has ingested over the preceding 24 hours – if an overdose is suspected then treatment with *N*-acetylcysteine should be commenced. There is little value in sending a paracetamol level when a staggered overdose has occurred.

A basic liver screen, including AST and serology for hepatitis A, B, C and E, HIV, as well as CMV and EBV, should be sent. You should also request an urgent abdominal ultrasound scan to assess the liver appearance and to look for pathology, such as a collection or a mass, as well as potential hepatic vein occlusion.

CASE PROGRESSION

The liver screen tests showed an elevated ferritin level of 1030 (normal range 22–275 $\mu\text{g/L}$) as well as an elevated alpha-fetoprotein level of 13 (reference range 0–5.8 kIU/L). The conjugated bilirubin level was 83 (reference range 0–4 $\mu\text{mol/L}$), in keeping with hepatocellular injury or biliary obstruction. An ultrasound scan of the liver identified no abnormalities. The virology screen was negative.

The INR gradually increased to 1.5 over the subsequent 48 hours. The gastroenterology team advised giving intravenous vitamin K in an attempt to correct the INR. A triple-phase computed tomography (CT) liver scan was arranged.

A consultant hepatologist reviewed the patient and took a focussed history. On direct questioning, the patient admitted to daily khat consumption, which he used as a stimulant during his nightshift work.

The CT scan showed possible inflammatory changes in the left lobe of the liver. A magnetic resonance imaging (MRI) scan was then performed, showing fibrotic changes throughout the left lobe of the liver (see [Figure 2.1](#), arrow points to left lobe of liver). A liver biopsy showed peri-portal collapse with lobular and portal inflammation, in keeping with an acute hepatitis and consistent with khat consumption.

Final diagnosis: Acute hepatitis secondary to khat consumption.

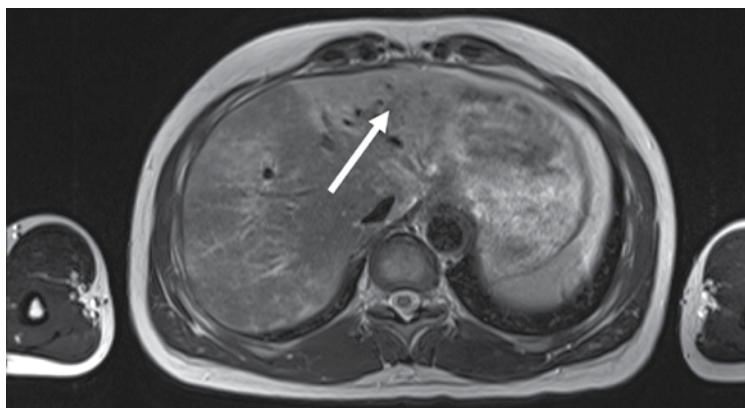


Figure 2.1 MRI scan of the liver showing fibrotic changes within the left lobe.

OUTCOME

The patient's INR level peaked at 1.7. He self-discharged prior to further management. He attended an outpatient clinic where he reported ongoing khat use. His liver function tests remain deranged.

CASE DISCUSSION

Khat is a flowering plant native to Northeast Africa. The leaves are chewed or made into pastes and teas where they are consumed for their stimulant properties. Khat is commonly used among Somalian communities throughout the world.

Khat contains the alkaloid, cathinone, which has amphetamine-like properties (stimulation and euphoria). Long-term khat consumption is associated with liver fibrosis – multiple studies have shown that khat generates reactive oxygen species and promotes hepatic cell apoptosis via mitogen-activated protein kinase (MAPK) activation. There is also an association between khat use and the development of ischaemic heart disease.

This case highlights the importance of taking a detailed drug and toxin history, asking specifically about recreational drugs. The patient did not admit to khat use until he was asked directly by the consultant gastroenterologist.

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CASE 3: YELLOW BLOOD

PATIENT HISTORY

A 45-year-old man was admitted with chest and abdominal pain. The pain had started gradually 12 hours earlier and had worsened throughout the day. The pain was located around the centre of his chest and upper abdomen and was described as constant and crushing in nature, radiating through to his back. At worst the pain was 8/10 in severity and associated with nausea. He described identical symptoms with previous episodes of pancreatitis. His past history also included hypertension and ischaemic heart disease. He took 25 mg atenolol OD, 2.5 mg ramipril OD, 75 mg aspirin OD, 40 mg simvastatin ON and 20 mg omeprazole OD. He lived alone, drank 280 units of alcohol weekly and was a smoker with a 40 pack year history.

EXAMINATION

Initial observations: T 36.4°C, HR 95 bpm, BP 120/74 mm Hg, RR 20 and SpO₂ 96% on room air.

The patient was alert but distressed due to ongoing pain. He was warm and well perfused, and appeared to be euvoelaemic. There was generalised abdominal tenderness with voluntary guarding throughout. Bowel sounds were of normal pitch. His chest sounded clear. There was no reproducible chest pain on palpation of the chest wall.

INITIAL RESULTS

Blood samples were taken in the emergency department, but the junior doctor reported that the blood appeared yellow when left to settle in the blood tubes (see [Figure 3.1](#)). The laboratory telephoned the emergency department to say that the blood was too lipaemic to allow a full blood count, potassium level or creatinine level to be processed. The only results that were available were as follows: Na 121, amylase 87, troponin T 64.

Electrocardiogram (ECG): normal sinus rhythm with Q waves in leads V4-V6 and II, III and AVF.

DIFFERENTIAL DIAGNOSES

The most likely cause of this patient's symptoms is acute-on-chronic pancreatitis. The patient describes similar symptoms during previous flares of pancreatitis and this would explain his abdominal pain. Although his amylase level is within the normal range, an elevated serum amylase only has approximately 80% sensitivity for identifying acute pancreatitis. Recent studies show that serum lipase has a higher specificity and sensitivity for acute pancreatitis than amylase.

Given the patient's chest pain and multiple cardiovascular risk factors (smoking history, hypertension and ischaemic heart disease), an acute coronary syndrome should be considered. His ECG shows ischaemic changes and the troponin T level is significantly elevated,



Figure 3.1 Lipaemic blood sample.

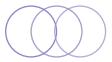
but in the context of a very lipaemic blood sample – interpretation of this result should be discussed with the biochemistry laboratory and the cardiology team on-call.

Chest pain radiating to the back raises the possibility of an aortic dissection. You should check for signs of radio-radial delay, a blood pressure difference between the left and right arm and a widened mediastinum on the chest radiograph.

Other causes of abdominal pain, such as a perforated peptic ulcer and cholecystitis should be considered.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient is in discomfort and will require analgesia. He should be kept 'nil by mouth' in case he requires surgical intervention, so intravenous paracetamol and opiates will be required, as well as intravenous fluids. He appears euvoelaemic and therefore does not need rapid fluid replacement. He is hyponatraemic according to the blood sample and therefore 0.9% sodium chloride at a rate of 125 mL/hr can be commenced, but his serum sodium level will need to be closely monitored to ensure that it does not increase or fall rapidly over the next few hours. Also be aware the serum sodium reading may not be accurate in the context of a lipaemic sample.



An erect chest x-ray should be performed to look for evidence of a perforated viscus (air under the diaphragm) or a widened mediastinum. His ECG will need to be repeated to monitor for any dynamic ischaemic changes, indicative of acute coronary syndrome. The case should be discussed with the cardiologists regarding whether treatment with dual antiplatelet therapy +/- heparin is indicated, particularly as the patient may require surgery, depending on the cause of his symptoms. A surgical review should also be requested in view of his abdominal pain, as well as imaging studies, such as an abdominal ultrasound scan or a computed tomography (CT) scan of the abdomen.

The laboratory technician will need to be contacted to discuss how further samples of blood may be processed. His potassium level, in particular, needs to be measured urgently. In view of his lipaemic blood sample, a total cholesterol and lipid profile should be sent.

Lastly the patient has a history of excessive alcohol intake. The ward staff will need to monitor for signs of alcohol withdrawal and treat this with benzodiazepines, if required. In view of his lifestyle, he is likely to have a poor diet and therefore vitamin B (B₁, B₂, B₃ and B₆) replacement therapy must be prescribed to prevent the development of Wernicke's encephalopathy.

CASE PROGRESSION

Over the next few hours, the patient developed marked epigastric pain and vomiting. An erect chest x-ray showed clear lung fields, a normal appearance of the mediastinum, with no free air under the diaphragm. His lipid profile results were as follows: total cholesterol, 21 (reference range 3.5–5 mmol/L); high-density lipoprotein (HDL), 0.86 (reference range >1 mmol/L); low-density lipoprotein (LDL), unable to be measured; and triglycerides, 81 (reference range <1.7 mmol/L). The cardiology team explained that the elevated troponin T level was difficult to interpret in the context of very lipaemic samples and that dual antiplatelet and heparin therapy should be withheld as a diagnosis of pancreatitis was more likely than an acute coronary syndrome.

An urgent abdominal ultrasound was performed, but poor views were obtained due to patient discomfort. The surgical and gastroenterology teams agreed that the likely diagnosis was acute-on-chronic pancreatitis secondary to hyperlipidaemia. Broad-spectrum antibiotics were commenced to cover for possible biliary sepsis. A CT scan of the abdomen showed pancreatitis with probable necrosis of the pancreatic head, chronic thrombosis of the superior mesenteric vein and portal vein, diffuse hepatic steatosis and gallstones.

The endocrinology team reviewed the patient and advised managing the hypertriglyceridaemia with an insulin infusion. The plan was to commence plasmapheresis (plasma exchange) if the patient did not improve. Over the following 24 hours, the triglyceride levels fell rapidly (see [Figure 3.2](#), a graph showing triglyceride levels following treatment with an insulin infusion), but the patient began to develop fevers and his blood results showed elevated inflammatory markers and progressively more deranged liver function. There was a tender, palpable mass in the right upper quadrant of the abdomen. These symptoms and signs were attributed to a combination of alcoholic hepatitis and a possible pancreatic abscess. Magnetic resonance cholangiopancreatography (MRCP) was attempted but was unsuccessful. Following antibiotics and fluid rehydration, the patient gradually improved.

Final diagnosis: Hyperlipidaemia causing an acute flare of pancreatitis.

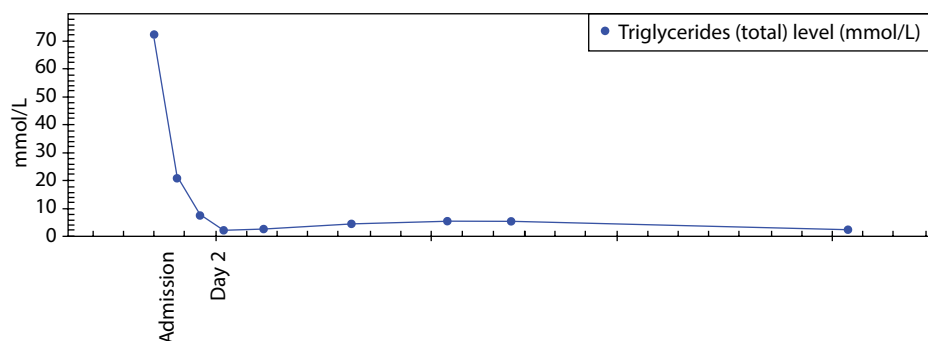


Figure 3.2 The graph shows serum triglyceride levels. Note the rapid reduction once the insulin infusion was commenced.

OUTCOME

The patient made a good recovery over the following weeks and was eventually discharged home. He has since re-presented with acute flares of pancreatitis on several occasions but has not had a recurrence of hyperlipidaemia.

CASE DISCUSSION

Prolonged alcohol misuse is a risk factor for developing severe hypertriglyceridaemia, as alcohol transiently increases serum triglyceride levels. In this case, the hypertriglyceridaemia was driving an acute flare of pancreatitis. The first-line treatment in such situations is an insulin infusion, which will activate lipoprotein lipase activity and break down chylomicrons. Heparin may also be given, as this stimulates further release of endothelial lipoprotein lipase. If this is unsuccessful, plasmapheresis may be necessary.

One of the main challenges with this patient was the difficulty in interpreting his initial blood results due to the very lipaemic samples. Hyperlipidaemia can cause a pseudohyponatraemia – in this case the sodium level was initially recorded as 121 mmol/L but may have been significantly higher. The laboratory technician on-call was able to manually process further blood samples thus allowing some results, including an INR level, to be obtained.

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CASE 4: AN UNUSUAL METHOD OF DELIBERATE SELF-HARM

PATIENT HISTORY

A 23-year-old chemistry student was admitted to hospital complaining of headache, nausea and shortness of breath. She was a reluctant historian, but the junior doctor taking the history managed to elicit that she had experienced fevers and nausea for around 48 hours and now had worsening shortness of breath on minimal exertion. The patient was well known to have a long history of depression with multiple emergency department attendances following episodes of deliberate self-harm. These had included mixed overdoses of drugs, such as sertraline, paracetamol and zopiclone, as well as self-inflicted wrist and forearm lacerations. On direct questioning, she admitted that she had 'done something a while ago' but refused to clarify this further. She had no further past medical history and was currently on no regular medications. She lived alone and had no current sexual partners. She denied any history of smoking or alcohol intake.

EXAMINATION

Initial observations: T 38.3°C, HR 105 bpm, BP 130/74 mm Hg, RR 26 and SpO₂ 98% on room air.

The patient was alert and orientated. She was warm to touch and appeared flushed. Heart sounds were normal and the patient was euvoelaemic. Her chest sounded clear. The abdomen was soft with mild, generalised discomfort. A neurological examination identified bilateral lower limb paraesthesia and an intention tremor in both hands. There was an area of erythema over the right antecubital fossa (see [Figure 4.1](#)).

INITIAL RESULTS

Routine blood tests: WCC 12.3, N° 9.2, Hb 141, Plt 580, Na 137, K 4.2, Creat 68, Bili 18, ALT 24, ALP 44, CRP 55, INR 1.1.

Chest x-ray: bilateral high-density infiltrates throughout the lung fields, with further lesions seen in the right ventricle (see [Figures 4.2](#) and [4.3](#)).

DIFFERENTIAL DIAGNOSES

The patient's main symptoms are fever, tachycardia, shortness of breath and nausea. This could represent a simple lower respiratory tract infection or a generalised viral illness, but the patient admits to an episode of deliberate self-harm preceding onset of symptoms. She is unwilling to give any further details and every effort should be made to persuade her to tell us whether she has ingested a harmful substance, particularly as the patient has access to many chemical agents.

The area of erythema over the right antecubital fossa looks like mild cellulitis and there is a visible puncture site – it appears that something may have been injected at this site recently.

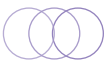


Figure 4.1 Erythema of the antecubital fossa.

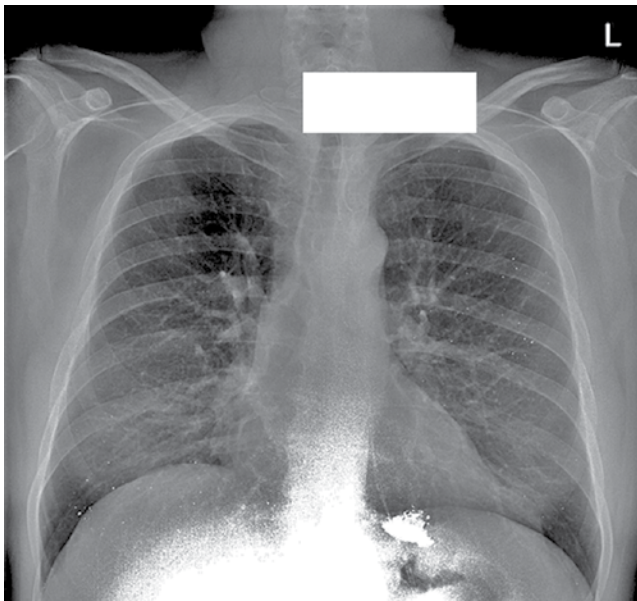


Figure 4.2 Chest x-ray showing high-density infiltrates throughout the lung fields.

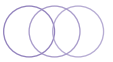


Figure 4.3 Chest x-ray showing further deposits present within the right ventricle.

The chest x-ray shows multiple high-density opacities throughout the lung fields and at the base of the right ventricle. The density of these lesions is in keeping with metallic deposits. This therefore raises the possibility that the patient has injected herself with a metallic compound.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient is tachycardic and febrile with elevated inflammatory markers. She has a clear area of cellulitis over the right antecubital fossa as well as evidence of pneumonitis on the chest x-ray. You should commence broad-spectrum antibiotics once a septic screen has been performed.

As it is currently unclear whether the patient has ingested or injected herself with a harmful substance, blood samples should be sent to test for the presence of paracetamol, salicylate, lead, lithium, iron and mercury. The National Poisons Information Service or on-call toxicology clinician (where available) can be contacted for further advice. A blood film may show basophilic stippling with lead and arsenic poisoning. Urine should be collected and sent for a toxicology screen.

If the patient becomes more unwell, treatment for heavy metal poisoning may need to be commenced despite no clear indication of what the patient has self-administered.

CASE PROGRESSION

Following further questioning, the patient admitted that she had self-injected with elemental mercury several days earlier. An x-ray of the right elbow was taken to identify any potential subcutaneous mercury deposits – there were none seen.

Her oxygen saturations fell to 94% on room air and an arterial blood gas showed mild type 1 respiratory failure. Her peak expiratory flow rate was monitored and showed no deterioration.



She required oxygen therapy for 48 hours. A computed tomography (CT) pulmonary angiography showed multiple metallic deposits and probable mercury-related pneumonitis.

The patient's renal and liver function was monitored daily with no deterioration. Both her blood and urine showed high levels of mercury. She commenced chelation therapy with 2,3-dimercapto-1-propanesulphonic acid (DMPS) – an agent that forms complexes with heavy metals, such as mercury and lead. After being declared medically fit for discharge, the psychiatry team took over further care of the patient.

Final diagnosis: Mercury toxicity.

OUTCOME

The patient made a good recovery but has continued to experience chronic abdominal pain since discharge. She has been followed up as an outpatient and has had no further hospital admissions.

CASE DISCUSSION

Mercury is highly toxic and where exposure is suspected, cases should immediately be discussed with specialist toxicology clinicians. This patient presented several days after mercury poisoning, having developed an area of cellulitis at the site of injection and a pneumonitis. She was at risk of developing a severe acute lung injury and large, life-threatening pulmonary emboli; however, her respiratory function recovered over the following days. Metallic mercury is occasionally used in traditional herbal medicines and poisoning has been reported via both oral and intravenous routes. In cases where mercury is injected, local necrosis around the injection site may develop, requiring extensive debridement.

Mercury exposure can cause thickening of the glomerular basement membrane resulting in nephrotic syndrome as well as renal tubular dysfunction. This patient's renal function was closely monitored for several days as an inpatient, and at regular intervals in the community without any evidence of deterioration. Aside from an intention tremor and mild paraesthesia, the patient displayed no features of neurological damage, which can include slurring of speech, ataxia and the development of peripheral neuropathy. Personality change and memory loss may also occur in acute mercury toxicity.

In cases such as this where patients have been exposed to toxic chemicals, it is important to ensure the safety of others who may encounter the agent(s). The National Poisons Information Service should be able to provide further support as to the need for personal protective equipment and consideration of other individuals who may have been exposed.

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CASE 5: SUDDEN-ONSET HEADACHE

PATIENT HISTORY

A 29-year-old man from New Zealand was on holiday in London. While passing urine he developed a sudden-onset occipital headache that came on over 1–2 seconds. At the onset of the headache, the patient described hearing a loud banging noise in both ears. He collapsed to the floor and was unable to stand up. He attempted to use his mobile phone to call for help but found that he was unable to move his right arm, which he described as feeling ‘heavy and numb.’ He developed slurred speech, blurring of vision and vomiting. He was found by a relative who called the ambulance service. His past medical history included migraines, which he said were typically left-sided posterior headaches preceded by a visual aura. He took no regular medications. There was no family history of intracranial bleeding or polycystic kidney disease. The patient worked as a dog groomer. He had never smoked, occasionally drank alcohol and denied any recreational drug use.

EXAMINATION

Initial observations: T 36.5°C, HR 80 bpm, BP 102/62 mm Hg, RR 18, SpO₂ 99% on room air.

Cardiovascular, respiratory and abdominal examinations were unremarkable. Neurological examination identified bilaterally reactive pupils with asymmetry, the left being 4 mm and the right 3 mm in diameter. Other positive findings included a left pronator drift and reduced co-ordination in the right lower limb. He was re-examined 4 hours later by one of the medical junior doctors who elicited a broad-based gait but no other neurological deficit.

INITIAL RESULTS

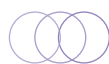
Routine blood tests: WCC 13.6, N^o 10.2, Hb 139, Plt 204, Na 136, K 3.6, Creat 75, CRP 4, INR 1.1.

CT head scan (without contrast): no abnormalities detected.

DIFFERENTIAL DIAGNOSES

The patient has a known history of migraines – his migraines had previously involved a left-sided posterior headache preceded by a visual aura. Migraines can vary in character, and it is not uncommon for neurological deficits, which may, in some cases, include limb weakness, to develop during a severe attack.

This headache came on instantly rather than progressively, suggestive of a vascular event such as a subarachnoid haemorrhage. The classic presentation of subarachnoid haemorrhage is a sudden-onset ‘thunder-clap’ to the back of the head, often associated with vomiting. A computed tomography (CT) head scan is a highly sensitive and specific test for subarachnoid bleeding, but the fact that this scan did not show evidence of a bleed does not exclude the possibility of a small haemorrhage. So-called ‘herald bleeds’ are small



subarachnoid haemorrhages that may precede a much larger bleed several days or weeks later.

An ischaemic stroke is unlikely in such a young patient and there was no evidence of this on the CT head scan. Cocaine abuse can precipitate an ischaemic stroke by causing vasospasm of the cranial arteries, but this patient denies the use of recreational drugs.

A space-occupying lesion with spontaneous bleeding is another possible diagnosis. A non-contrast CT would pick up the majority of larger lesions, but if there is a high index of suspicion then a contrast CT scan or magnetic resonance imaging (MRI) should be considered.

Vertebral artery dissection can develop following trauma but may not present until days, or weeks after the event. Symptoms include a sudden-onset occipital headache, often associated with nuchal pain and vomiting. Unilateral cranial nerve impairment may also develop.

Although there was no history of recent trauma, the patient may have neglected to mention an event that occurred several days or weeks earlier.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

Analgesia and anti-emetics should be given initially. A probable diagnosis is that the patient has had a subarachnoid bleed. A lumbar puncture should be performed to identify xanthochromia in the cerebrospinal fluid (CSF). It takes at least 2 hours for the haemoglobin to degrade and be detected as xanthochromia in the CSF and the lumbar puncture should ideally be performed at least 12 hours after the onset of the headache to increase the sensitivity of the test. A positive result becomes increasingly unlikely after 10 days post-event and a magnetic resonance imaging (MRI) scan may need to be performed at this stage to identify the presence of old blood in the subarachnoid space.

If the lumbar puncture is negative for xanthochromia, a diagnosis of subarachnoid haemorrhage is very unlikely and the case should be discussed with a neurologist. A trial of triptan medications may be considered to treat a possible severe migraine. Triptans are agonists to the serotonin 5-HT_{1B} and 5-HT_{1D} receptors that cause vasoconstriction of cranial vessels and inhibit the release of pro-inflammatory neuropeptides. A trial of high-dose steroids may also be used for the treatment of refractory migraine.

CASE PROGRESSION

Following the normal CT brain scan, a lumbar puncture was performed 12 hours after the onset of the headache. There was no evidence of xanthochromia. The patient continued to describe a very mild reduction in sensation over the V1-V2 distribution of the right trigeminal nerve distribution and a heavy sensation in the right lower limb, although tone and power remained normal when objectively assessed.

A MRI/magnetic resonance angiography (MRA) scan was arranged. This showed bilateral posterior cerebral artery infarctions (see [Figure 5.1](#)).

The patient's care was transferred to a hyperacute stroke unit where he commenced 300 mg aspirin once daily for 2 weeks and subsequently switched to 75 mg clopidogrel once daily, which was planned to continue indefinitely. Carotid Doppler studies were unremarkable.

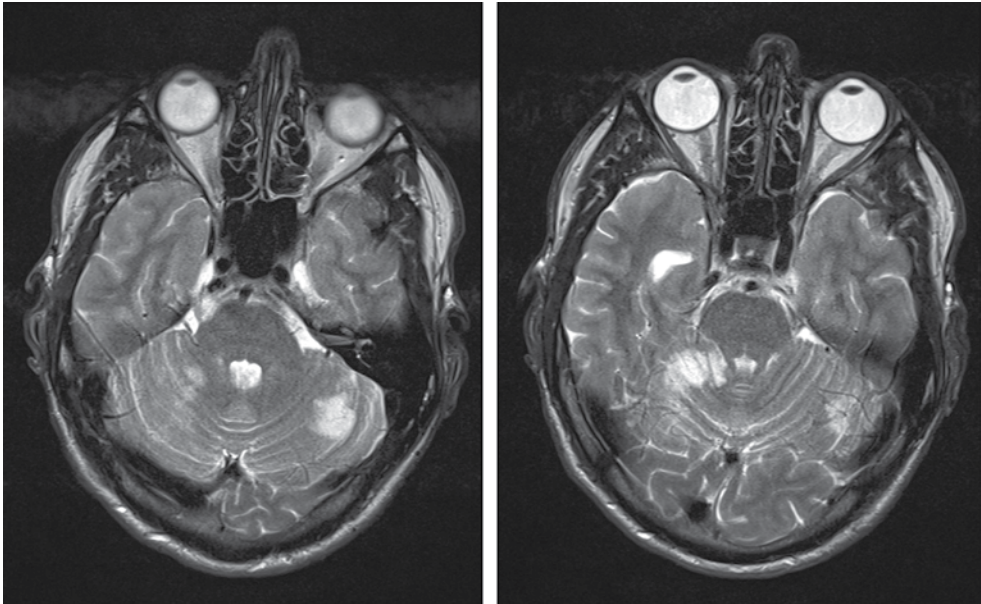
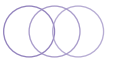


Figure 5.1 MRI brain scan showing bilateral posterior cerebral artery infarctions.

A transthoracic echocardiogram revealed no abnormalities, but a bubble echocardiogram identified a patent foramen ovale (PFO).

Final diagnosis: Bilateral posterior cerebral artery infarctions secondary to a PFO and a presumed deep vein thrombosis.

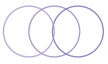
OUTCOME

With specialist neuro-physiotherapy the patient made a full recovery. He returned home to New Zealand where further treatment options for his PFO will be considered.

CASE DISCUSSION

When any patient presents with evidence of an ischaemic stroke, basic investigations including an electrocardiogram (looking for arrhythmias such as atrial fibrillation), an echocardiogram and bilateral carotid Doppler studies should be performed to identify an underlying precipitant of the event.

This patient was found to have a PFO. He probably had a subclinical deep vein thrombosis, possibly related to his recent long-haul flight to London. With normal anatomy, the thrombus may travel through the venous system to the right side of the heart and into the pulmonary circulation forming a pulmonary embolus. Where there is a PFO, the thrombus can pass into the left side of the heart and into the arterial circulation, causing a stroke. This is termed a *paradoxical embolism*.



The patient will continue on antiplatelet therapy while further treatment options, such as surgical closure of the PFO, are considered.

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CASE 6: A HYPERTENSIVE PATIENT WITH CARPAL SPASMS

PATIENT HISTORY

A 43-year-old man presented to the emergency department while in police custody, having developed painful, bilateral wrist spasms shortly after being arrested. He reported experiencing several similar episodes with spasms of the wrist and forearms, associated with perioral tingling over recent months. The episodes usually coincided with episodes of anxiety or distress. He had been experiencing headaches regularly over the past 5 years. On direct questioning, he also described recent symptoms of polydipsia and polyuria, drinking around 4 litres of water per day and waking to urinate 5–10 times per night. He denied any other medical history and took no regular medications. He was a current smoker of 20 cigarettes daily and drank around 60 units of alcohol per week. He admitted to daily cannabis use and occasional cocaine use.

EXAMINATION

Initial observations: T 36.1°C, HR 96 bpm, BP 204/104 mm Hg (similar readings in both arms), RR 24 and SpO₂ 99% on room air.

On examination, the patient appeared agitated but was orientated to time, place and person. He was clinically euvoalaemic. His blood pressure was persistently elevated and he had a mild tachycardia. There were no audible cardiac murmurs. His chest was clear. His abdomen was soft and non-tender with no palpable organomegaly. Fundoscopy identified silver wiring, cotton wool spots and flame haemorrhages but no papilledema. There were no carpal spasms at the time of examination.

INITIAL RESULTS

Routine blood tests: WCC 8.3, Hb 148, Plt 278, Na 145, K 2.2, Creat 145, CRP 6.

Arterial blood gas (performed on room air): pH 7.53, pO₂ 12.2, pCO₂ 3.4, BE +2.1, HCO₃ 36, lac 1.9, Na 142, K 1.7, glucose 5.4.

Electrocardiogram (ECG) showed sinus rhythm with U waves (see [Figure 6.1](#)).

DIFFERENTIAL DIAGNOSES

The patient describes symptoms of polydipsia and polyuria – this is suggestive of possible diabetes mellitus. The patient has severe hypertension with grade 3 hypertensive retinopathy. He could have an underlying metabolic syndrome, with early onset of cardiovascular disease.

His ECG is abnormal with U waves in all leads, particularly clear in the anterolateral leads (see [Figure 6.1](#), U wave is circled). This is a sign that develops in profound hypokalaemia. Hypokalaemia in patients with hypertension should prompt you to think of hyperaldosteronism, particularly in the context of a metabolic alkalosis. Primary hyperaldosteronism

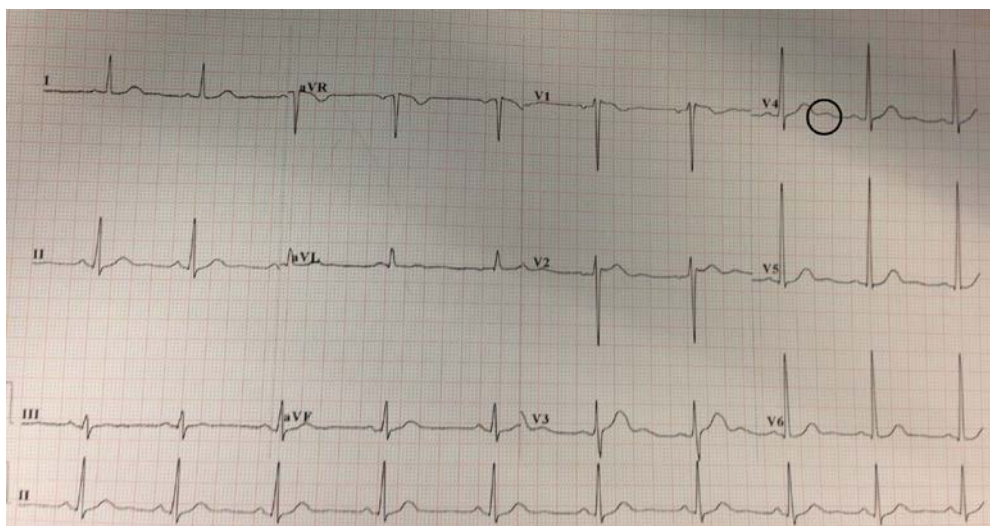


Figure 6.1 ECG showing U waves (circled), indicative of hypokalaemia.

develops when the adrenal glands produce excess aldosterone, due to adrenal hyperplasia or adenoma/microadenoma formation. Secondary hyperaldosteronism is due to inappropriate activation of the renin–angiotensin–aldosterone system, e.g. when renovascular disease is present, leading to high circulating levels of aldosterone.

The intermittent episodes of carpal spasm could be due to myoclonic epilepsy, as patients experience recurrent jerks or twitching of muscle groups. This form of epilepsy typically presents in childhood or early adulthood. Patients remain conscious and alert throughout the seizure. Seizures may be exacerbated by electrolyte imbalances – in this case the hypokalaemia could be a precipitant.

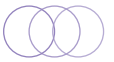
Hypocalcaemia can present with neuromuscular complications, such as painful tetany of the hand and foot muscles. This may develop secondary to hypoparathyroidism, but in view of the patient's low potassium level, if hypocalcaemia is present then an eating disorder or metabolic disease should also be suspected.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient's symptoms of carpal spasm have resolved at present. His electrolytes should be checked and if he was hyperventilating at the time that the arterial blood gas sample was taken then this can be repeated once he is less agitated (an increased respiratory rate [RR] will increase removal of carbon dioxide).

With regard to his hypertension, there is no indication to treat this as an emergency, as he has no symptoms of neurological deficit (headache, visual disturbance or impaired consciousness), aortic dissection or cardiac ischaemia. The aim should be to gradually reduce his blood pressure over the next few days, aiming for no more than a 25% reduction in his mean arterial pressure over the first 24 hours.

This patient will require immediate potassium replacement therapy. He should have continuous cardiac monitoring while intravenous potassium is delivered, due to the high risk of



cardiac arrhythmias developing. The myocardium is extremely sensitive to low circulating potassium levels; ventricular arrhythmias and cardiac arrest can result, in addition to the ECG changes already observed in this patient. Potassium chloride can be administered safely at a rate of up to 10 mmol per hour, and so a 1 L bag of 0.9% sodium chloride with 40 mmol potassium chloride can be prescribed to run over 4 hours. If the serum potassium level is ≤ 2 mmol/L then the potassium infusion should be run in a high dependency unit setting to allow close monitoring of the patient and frequent electrolyte levels to be taken. A central line will be required if more concentrated doses of potassium are used, in order to avoid thrombophlebitis. The team may prefer to use concentrated doses of potassium to avoid excessive intravenous fluids in this hypertensive patient.

The patient's serum magnesium level should also be checked as hypomagnesaemia may lead to refractory hypokalaemia by inhibiting ATP-dependent potassium channels and increasing potassium secretion. If hypomagnesaemia is present, magnesium and potassium will need to be replaced simultaneously.

CASE PROGRESSION

The patient was admitted to the high dependency unit to receive potassium replacement. When his serum potassium level had normalised, he was monitored for a further 24 hours. His potassium level was re-checked at this point and was found to be low again. He was prescribed oral potassium replacement tablets in addition to a slow infusion of intravenous potassium chloride.

The patient commenced amlodipine (5 mg OD initially, increased to 10 mg OD the following day) plus 2.5 mg bisoprolol OD to treat his blood pressure, which settled at around 150/96 mm Hg over the next 2 days.

Plasma renin and aldosterone levels were taken. The aldosterone level was markedly elevated and the renin level was low. A computed tomography (CT) scan of his adrenals showed a 3.4×2.8 cm enhancing left adrenal adenoma.

During his stay in hospital, the patient had an argument with his ex-wife. As his RR increased, he developed peri-oral tingling and his carpal spasms returned. A blood gas was repeated at the time and a metabolic alkalosis had developed once again. The endocrine team reviewed the patient and explained that he had primary aldosteronism (Conn's syndrome) leading to hypokalaemia and a chronic metabolic alkalosis. Whenever he hyperventilated, the alkalosis would worsen (due to a reduction in carbon dioxide levels) and his ionised calcium became less available to tissues, leading to the above symptoms of hypocalcaemia.

Final diagnosis: Primary aldosteronism.

OUTCOME

The patient was discharged and underwent a surgical resection of his adrenal adenoma 6 weeks later. His blood pressure has remained controlled and he has had no further episodes of hypokalaemia or carpal spasm since.



CASE DISCUSSION

The patient was found to have markedly elevated aldosterone levels, along with very low levels of renin. The likely mechanism was that as aldosterone levels increased, the circulating sodium level rose, leading to an increase in intravascular volume, triggering a reduction in renin production via a negative feedback loop within the renin–angiotensin–aldosterone axis, i.e. less renin was produced in an attempt to maintain homeostasis. In this case, primary aldosteronism had developed due to an aldosterone-secreting adrenal adenoma.

Primary aldosteronism should be suspected in young hypertensive patients or those with treatment-resistant hypertension. Renin and aldosterone levels should ideally be taken prior to anti-hypertensive therapy, where possible, as anti-hypertensive agents lead to changes in the renin–angiotensin–aldosterone axis, making results more challenging to interpret. In the majority of cases, however, patients are already established on several anti-hypertensive agents prior to investigation for aldosteronism.

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CASE 7: AN ELDERLY PATIENT ADMITTED WITH A FALL

PATIENT HISTORY

A 76-year-old woman was admitted to hospital after being found on the floor by her son. She was able to recall the event: she described standing from her chair and attempting to walk to the next room, when she lost her balance and fell backward. She denied any preceding loss of consciousness, chest pain or palpitations. She did not report sustaining any injuries. She was unable to get back up and so lay on the floor for approximately 1 hour prior to her son arriving and assisting her. There were no features of vertigo or light-headedness. She had been admitted with multiple falls over recent months, all with a similar history of losing balance prior to falling. She had attended the specialist falls clinic a few weeks earlier where she was diagnosed with a high level balance and gait disorder in the context of likely cerebral vascular disease. Her past medical history also included hypertension and hypercholesterolaemia. She took 5 mg ramipril OD and 20 mg simvastatin ON. She lived alone with no formal package of care, but her family visited several times daily. She had required increasing amounts of help at home lately due to difficulty mobilising and progressive cognitive impairment. She mobilised with a frame when supervised but tended not to use this when alone. She was independent with personal care but required help with meal preparation and cleaning. She was incontinent of urine and occasionally of faeces also. She had never smoked. Her son informed the junior doctors that the patient drank around 40–50 units of alcohol per week.

EXAMINATION

Initial observations: T 36.9°C, HR 76 bpm, BP 112/68 mm Hg, RR 14, SpO₂ 97% on room air.

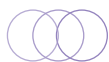
The patient was noted to demonstrate challenging and somewhat aggressive behaviour with male members of medical and nursing staff but was otherwise comfortable and settled. Her heart sounds were normal and her chest sounded clear to auscultation. Her lying and standing blood pressures were 142/78 mm Hg and 120/60 mm Hg, respectively. Neurological examination identified a broad-based, small stepping gait with reduced arm swing. There was a subtle increase in tone in all limbs and mild bradykinesia of the upper limbs. Power and reflexes were normal and there were no sensory abnormalities. Plantar responses were down going bilaterally. Her abbreviated mental test score (AMTS) was 8/10, losing points for counting down from 20 to 1 and recall.

INITIAL RESULTS

Routine blood tests: WCC 10.3, Hb 137, Plt 320, Na 135, K 3.8, Creat 89, CRP 3, INR 0.9, liver function tests (LFTs) normal.

Electrocardiogram (ECG): sinus rhythm, rate 70 bpm.

Urine dip: no abnormalities detected.



DIFFERENTIAL DIAGNOSES

This patient has been admitted following a fall. There are many complex causes of falls in elderly patients and it is important to be thorough when clerking such patients, for example establishing whether they have impairment of vision, difficulty with balance or limited movement, all of which may have precipitated the event. In this case, the patient states that she remembers the fall and describes feeling a preceding sensation of loss of balance but no loss of consciousness.

On examination, the patient was noted to have bradykinesia and mildly increased tone in the upper limbs. These could be features of Parkinson's disease, although there is no tremor present. Postural instability is a common feature of Parkinson's disease.

Multisystem atrophy (Shy-Drager syndrome) can also present with features of Parkinsonism along with autonomic dysfunction. Signs may include a postural drop in blood pressure (20 mm Hg fall in systolic blood pressure and 10 mm Hg fall in diastolic blood pressure are considered significant) and urinary incontinence, both of which are present in this patient. She has a degree of postural hypotension, but she may also have lower blood pressures in the hours immediately following anti-hypertensive administration, which could prompt a fall.

The patient drinks alcohol to excess, which is associated with an increased risk of progressive cognitive impairment and cerebellar ataxia. This may explain her broad-based gait and reduced AMTS score. She may also have been inebriated when she fell over.

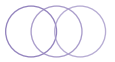
Neurological conditions must be considered. The patient could have experienced a transient ischaemic attack or a subtle stroke. Falls may be prompted by underlying neuropathies or myopathies, which a thorough neurological examination will identify. Normal pressure hydrocephalus (NPH) classically presents with the triad of gait disturbance, a predominantly frontal lobe dementia and urinary incontinence.

There are neither symptoms nor signs to suggest that a urinary tract infection may be present – this could also be a possible cause for the patient's recurrent falls with confusion and urinary incontinence. The urine dip test was unremarkable but this does not exclude a urinary tract infection, particularly if the sample was dilute or the patient had recently voided her bladder prior to collecting the sample. Many bacteria, such as enterococci, staphylococci and *Acinetobacter* are incapable of reducing nitrate to nitrite and a urine dipstick test is not always sufficient to identify infection with these organisms.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient will need some routine bloods to investigate for causes of confusion, including corrected calcium, thyrotropin (TSH), glucose and HbA1c levels, syphilis and HIV serology, and vitamin B₁₂ and folate levels.

A computed tomography (CT) head scan will help to identify whether there is significant pathology such as small vessel disease (this may be indicative of vascular dementia), dilated ventricles (due to conditions such as NPH), a subdural haematoma, or evidence of cerebral infection or malignancy.



A chest x-ray and urine culture should be performed to look for underlying infection. A physiotherapy assessment of her mobility should take place once the patient arrives on the ward. In view of her high alcohol intake, the patient will need to be monitored for signs of alcohol withdrawal and treated accordingly with benzodiazepines to prevent agitation and possible seizures. Vitamin B and thiamine replacement should be administered to prevent Wernicke–Korsakoff syndrome.

CASE PROGRESSION

The patient was seen by a specialist doctor from the elderly care team who performed an in-depth assessment, noting that the patient had poor executive function abilities, delayed recall and an impaired attention span. A magnetic resonance imaging (MRI) scan of the brain was requested, which showed severe NPH secondary to stenosis of the aqueduct of Sylvius (see [Figure 7.1](#)), which was likely to be chronic and partially compensated.

The patient was transferred to a neurosurgical unit where an endoscopic third ventriculostomy was performed. She developed a hospital-acquired pneumonia post-operatively but otherwise recovered well and was discharged home 3 weeks later.

Final diagnosis: Normal pressure hydrocephalus.

OUTCOME

The patient was reviewed 4 weeks post-discharge. Her gait had improved dramatically and she reported no further falls. She felt that she was thinking more clearly and was able to live more independently. Her AMTS had increased to 9/10. A ‘get up and go’ assessment (a series of manoeuvres to assess mobility) showed an improvement from 35 seconds pre-procedure to 15 seconds post-procedure. The patient was discharged from clinic and has remained well.

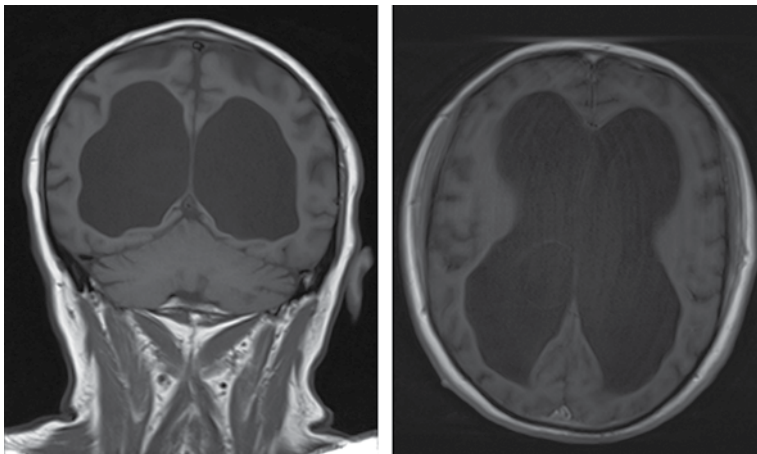


Figure 7.1 MRI brain scan demonstrating normal pressure hydrocephalus.



CASE DISCUSSION

NPH is a process whereby cerebrospinal fluid (CSF) accumulates within the cerebral ventricles, leading to an increase in intracranial pressure (ICP). The classic triad of symptoms may develop:

1. *Gait disturbance*: This is usually a slow, broad-based gait and may mimic Parkinsonian or ataxic movements.
2. *Cognitive impairment*: Memory loss and inattention are prominent features, although patients may present with frontal lobe symptoms of mood change, aggression and socially inappropriate behaviour.
3. *Urinary incontinence*: This is often the last feature to present, when NPH has become more severe. Patients develop a hyper-reflexic bladder due to sacral nerve involvement.

The diagnosis is usually made via CT and MRI imaging of the brain. If a lumbar puncture is performed, CSF pressure will be normal or slightly elevated. NPH typically develops in elderly patients and may be mistaken for Alzheimer's dementia or Parkinson's disease. In this case, a third ventriculostomy was performed, whereby neurosurgeons create a perforation within the third ventricle floor, thus diverting CSF flow. Patients who are not suitable for this procedure (based on anatomical considerations) will have a shunt inserted from the ventricle into the peritoneum (although other sites, such as the right atrium, may be used) to drain CSF. Depending on the severity and duration of NPH, patients have varying degrees of recovery post-shunt insertion.

As NPH is a potentially reversible cause of dementia; it is important to exclude this in all patients presenting with progressive cognitive impairment.

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CASE 8: A YOUNG MOTHER WITH CONSTIPATION

PATIENT HISTORY

A 22-year-old woman presented to hospital complaining of a 2-week history of fever, shivers and malaise. She had visited her general practitioner several times in the past fortnight, who had initially suspected that she had influenza. She had been experiencing intermittent frontal headaches associated with episodes of nausea. The patient denied any vomiting but had suffered from a constant, dull ache in the upper abdomen over the last few days. She had not experienced diarrhoea and could not recall opening her bowels during the preceding week. There were no symptoms of photophobia, neck stiffness or cough. She was normally fit and well with no past medical problems. She took no regular medications aside from a course of proguanil hydrochloride with atovaquone (anti-malarial prophylaxis) that she had recently completed. She lived with her husband and 14-month-old son, whom she was breastfeeding at the time of presentation. She had never smoked and did not drink alcohol. The patient and her family had returned 3 weeks earlier from a holiday in Ghana, where they had stayed for 2 weeks. They spent most of their holiday in Accra, but had travelled to rural areas for 3–4 days to visit relatives. Her husband had been well, but her son developed symptoms of fever and diarrhoea toward the end of the holiday. He had recovered fully and did not require any medical intervention. She had otherwise remained in the United Kingdom for the last 2 years, although she had lived in Ghana until she was 18 years old. The patient stated that her husband was her only sexual contact.

EXAMINATION

Initial observations: T 39.1°C, HR 60 bpm, BP 104/62 mm Hg, RR 16, SpO₂ 99% on room air.

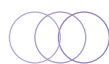
The patient appeared comfortable at rest and was haemodynamically stable despite her persistently high fever. There was no rash and no palpable cervical, axillary or inguinal lymphadenopathy. There was no oral candidiasis. Her chest was clear to auscultation. Her heart sounds were normal with a rate of 50–60 bpm. Her mucus membranes appeared dry. She had mild right and left upper quadrant tenderness with quiet bowel sounds. She was moving all four limbs normally and had no neck stiffness or photophobia.

INITIAL RESULTS

Routine blood tests: WCC 24.2, N^o 22.8, L^o 0.6, Hb 123, Plt 110, Na 135, K 3.7, Creat 78, Bili 42, ALT 220, ALP 88, INR 1, CRP 62.

DIFFERENTIAL DIAGNOSES

In a patient who has returned from Ghana with fevers and malaise and has thrombocytopenia, the first diagnosis to consider is malaria. *Plasmodium falciparum* infection is the



most common cause of malaria in Ghana, responsible for 90% of cases and can be fatal if left untreated. The patient states that she has taken a course of anti-malarials, but even with drug adherence there is still a risk of developing malaria. In any returning traveller a risk assessment for viral haemorrhagic fever is required.

HIV infection is another important diagnosis to consider. A seroconversion illness may develop around 6 weeks after HIV exposure, presenting with fever and non-specific constitutional symptoms.

The liver function tests show a hepatic picture with an elevated ALT. The patient has symptoms of fever and abdominal pain, suggesting a possible acute hepatitis. Hepatitis A is typically contracted via the faecal–oral route and there are widespread outbreaks throughout Ghana; however, if she grew up in Ghana she is likely to have had this as a child and to now be immune. Hepatitis B and C infections may have been contracted through sexual contact or other body fluid exposure. Hepatitis E can present in a similar manner to hepatitis A and should be considered.

Yellow fever is endemic in Ghana and is usually transmitted by the *Aedes aegypti* mosquito. It is often a relatively mild illness with influenza-like symptoms of fever, headache, myalgia and vomiting. Patients with more severe infections may develop jaundice and occasionally gastrointestinal haemorrhage. Other tropical infections, including enteric fever, brucellosis, dengue fever, chikungunya and rickettsial infection should also be considered.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

In view of the deranged liver function tests and the patient's abdominal pain, a liver screen should be performed, including an abdominal ultrasound scan.

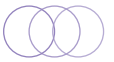
Malaria testing should be performed urgently and, if negative, should be repeated daily until she has had three negative tests. A full septic screen should be performed, with three sets of blood cultures taken (inform the lab of the travel history) a urine sample and a stool sample for culture. A chest x-ray should be performed. Routine testing should include an HIV test. A p24 antigen test is now available in many hospitals, allowing more accurate identification of primary HIV infection (seroconversion). The patient should be isolated and barrier nursed in view of her travel history. Liaise with the infectious diseases team regarding testing and appropriate treatment of potential tropical diseases.

CASE PROGRESSION

The patient remained persistently febrile over the next 24 hours with no clear indication as to the source of her infection. Blood films were negative for malaria. She was started on metronidazole and co-amoxiclav by the physicians caring for her, to provide broad-spectrum cover for an unknown infection. An abdominal ultrasound scan was unremarkable.

Her inflammatory markers remained elevated and a chest x-ray showed no focal consolidation. She remained constipated until multiple laxative agents were administered. She was reviewed by the surgical team who could identify no cause for her abdominal tenderness and fever. A computed tomography (CT) scan of her abdomen and pelvis was advised.

By 48 hours, her blood cultures were growing gram-negative rods. The patient was reviewed by the infectious diseases team who felt that typhoid fever was the likely diagnosis. Her



antibiotic regime was switched to ceftriaxone and her fever settled over the next 24 hours. Her blood cultures ultimately grew *Salmonella enterica* typhi.

Final diagnosis: Typhoid fever.

OUTCOME

The patient made a good recovery with the course of ceftriaxone and was discharged from hospital 3 days later. Due to the timing of the illness and the incubation period of typhoid, the infectious diseases team felt that it was possible that the patient's son had contracted typhoid fever toward the end of their stay in Ghana and the patient had subsequently contracted it from him shortly after arriving back home to the United Kingdom. As ceftriaxone is present in low concentrations in breast milk, the patient opted to discontinue breastfeeding. She was advised against preparing food for her family until her symptoms had resolved.

CASE DISCUSSION

Typhoid fever is a bacterial disease that is common in areas of poor sanitation within Asia, Africa and Latin America. It is usually spread via the faecal–oral route and can vary greatly in severity.

Classically during the first week of infection, the patient develops a persistently high fever (39–40°C) with features of non-specific malaise and abdominal pain.

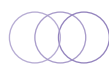
By the second week, rose spots (erythematous macular lesions secondary to bacterial emboli) may form over the chest and abdomen, and tender hepatosplenomegaly develops. Blood tests show an acute hepatitis. A progressive delirium may emerge.

During the third week, patients may develop intestinal haemorrhage and seeding of infection, with abscesses developing throughout the abdomen and a high risk of endocarditis.

A 'relative bradycardia' is common in typhoid fever and is demonstrated in this patient. This is a comparatively low heart rate despite signs of profound sepsis (fever, hypotension and delirium). The underlying mechanisms of a relative bradycardia in the context of infectious disease are poorly understood. The sign may be present in dengue fever but is more commonly seen in typhoid fever, Legionnaire's disease and pneumonia caused by *Chlamydia* sp. A relative bradycardia has not been shown to be present in other infections caused by salmonella bacteria, and is most often observed in infections where the causative bacteria are both gram-negative and intracellular.

The patient had symptoms of constipation – diarrhoea is a more common feature of typhoid fever, with between 20% and 50% of patients developing this symptom during the course of their illness. Classically the appearance of the diarrhoea is described as 'pea-green soup'. Diarrhoea is seen more frequently among younger patients, whereas adult patients may continue to have normal bowel motions or even develop constipation.

With thanks to Dr Anna Goodman for her help with this case.



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CASE 9: ARTHRITIS, MISCARRIAGE AND DROWSINESS

PATIENT HISTORY

A 28-year-old schoolteacher was brought to hospital by her husband, who described a 5-hour history of acute disorientation, drowsiness and incomprehensible speech. She had been generally unwell over the preceding week, with symptoms of intermittent fevers, chills, headache, nausea and malaise. She was usually fit and well, although she had attended hospital twice in the past 12 months – first for a spontaneous miscarriage 6 months earlier that occurred 18 weeks into the pregnancy and second for an acutely swollen knee that was aspirated in the emergency department 3 months ago. She took no regular medications. She had never smoked and did not drink alcohol. She was originally from Dubai but had lived in the United Kingdom for the past 20 years. She had last travelled to Dubai 10 months earlier to visit family. She had also visited Switzerland and Austria over the preceding month, where she had been trekking through the countryside.

EXAMINATION

Initial observations: T 37.6°C, HR 88 bpm, BP 116/70 mm Hg, RR 14, SpO₂ 100% on room air.

The patient was difficult to engage and examination was therefore limited. She appeared euvolaemic, had normal heart sounds and had no peripheral stigmata of endocarditis. Her chest was clear to auscultation. Her abdomen was soft and non-tender. No rashes were seen and there was no palpable cervical or axillary lymphadenopathy. Her Glasgow Coma Scale (GCS) score was 11/15 (E3 V3 M5). Cranial nerve examination was limited, but there was no obvious facial asymmetry and pupils were equal in size and reactive to light. Fundoscopy was not performed. Tone and reflexes were normal in all four limbs and plantars were down going. She was drowsy and intermittently mute throughout the clerking.

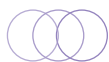
INITIAL RESULTS

Routine blood tests: WCC 3.3, N^o 1.2, L^o 1.7, Hb 108, MCV 72, Plt 238, Na 140, K 3.7, Creat 61, CRP 3.

Chest x-ray: clear lung fields.

DIFFERENTIAL DIAGNOSES

The patient is confused and, given the prodrome of fever, delirium and encephalitis are likely diagnoses. The multiple causes of encephalitis are classically categorised into viral, bacterial, protozoal and autoimmune. Common causes of viral encephalitis include herpes simplex virus (HSV), varicella-zoster virus (VZV) and HIV. Cytomegalovirus (CMV) and Epstein–Barr virus (EBV) can also cause acute encephalitis. Tick-borne encephalitis (perhaps as a



feature of Lyme disease) is a possibility, particularly given the recent history of trekking in Austria. Bacterial encephalitis can develop in patients with exposure to tuberculosis (TB), mycoplasma, syphilis and chlamydia. Toxoplasmosis and amoebiasis are associated with the development of encephalitis, but this is uncommon.

Delirium may be precipitated by a wide range of pathologies, including urinary and respiratory infections, disseminated sepsis, or bacteraemia. Endocarditis needs to be considered in view of the recent knee effusion.

Cerebral systemic lupus erythematosus (SLE) can present with psychosis and focal neurological signs. An underlying SLE/antiphospholipid (APLS) picture could explain her altered neurological state as well as her recent history of second trimester miscarriage and arthropathy.

An intracerebral space-occupying lesion (e.g. tumour or abscess) may account for the patient's drowsiness and low-grade fever. Another consideration is paraneoplastic encephalitis, for example anti-*N*-methyl-D-aspartate (NMDA) receptor encephalitis may be present – particularly if there is an underlying lung, ovarian or breast malignancy.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

A full septic screen, including three sets of blood cultures and a mid-stream specimen of urine (MSU), should be sent to the lab. The urine dipstick result should be reviewed in case of microscopic haematuria or nitrite and tested for β -HCG to exclude pregnancy. A computed tomography (CT) brain scan should be performed urgently to look for evidence of intracerebral pathology.

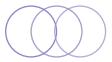
Aciclovir and broad-spectrum antibiotics with high cerebrospinal fluid (CSF) penetration, such as ceftriaxone, should be started within an hour. A lumbar puncture will need to be performed as soon as possible to send CSF samples for cytology, microscopy and culture, protein levels, glucose levels and virology testing.

The history was taken from her husband. In this case, we need further information to establish a diagnosis and it may be that the events that he described, of a miscarriage and arthropathy, are linked to this presentation. The history should be confirmed and further clarified with notes from her previous hospital admissions. The junior doctors on-call at the relevant hospitals should be contacted and asked to provide any case notes or results available from electronic records. The hospital secretaries and clerks may be able to assist with getting copies of her case file sent to you.

CASE PROGRESSION

A CT brain scan performed overnight showed no abnormal pathology. The on-call junior doctor commenced ceftriaxone and aciclovir to cover for possible meningitis or encephalitis. A lumbar puncture was performed; unfortunately the opening pressure was not documented. The CSF results were as follows:

- WCC 217×10^6 (98% lymphocytes; reference range $0-5 \times 10^6/L$), RBC 2×10^6 (reference range $0-10 \times 10^6/L$), protein 0.78 g/L ($0-0.44$ g/L), glucose 2.1 mmol/L (plasma glucose 5.1), LDH 65
- CSF smear: Negative for acid-fast bacilli
- Gram stain: Negative for bacterial organisms



An HIV test was negative. The patient continued to spike low-grade fevers for the next 24 hours. She was examined by a consultant who noted bilateral papilloedema on fundoscopy. Forty-eight hours later, the CSF polymerase chain reaction (PCR) results came back as negative for HSV, VZV, enterovirus, parechovirus and adenovirus negative. A cerebral magnetic resonance venogram showed no evidence of cerebral venous sinus thrombosis. The autoimmune screen was unremarkable.

She was reviewed by the neurology team who recommended multiple tests, including ammonia, vitamin B₁₂, folate and thyroid-stimulating hormone levels, all of which were within the normal ranges. A repeat lumbar puncture was performed to send CSF for analysis of voltage-gated potassium channel autoantibodies, which are associated with limbic encephalitis.

The patient's blood culture samples were sterile at 6 days and the ceftriaxone and aciclovir were stopped at this point. A magnetic resonance imaging (MRI) scan with contrast of her brain and spine was performed but showed no signs of hyperintensity suggestive of encephalitis or foci of infection.

By the tenth day of admission, the patient was becoming increasingly alert and orientated. She was keen to return home. Her papilloedema was significantly reduced and she showed no focal neurology. She remained afebrile and was felt to be medically fit for discharge by day 12 of her admission. Although no clear diagnosis was established, she was back at her baseline function and was thus discharged to be followed up as an outpatient by both the infectious diseases and neurology teams.

A sample of CSF obtained on the day of admission had been placed in a tuberculosis (TB) culture bottle 6 days after it was obtained. Unexpectedly, 14 days after the patient had presented, this sample was found to be growing gram-negative coccobacilli that were eventually cultured as *Brucella melitensis*.

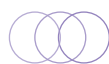
Final diagnosis: Neurobrucellosis (*Brucella melitensis* meningoencephalitis).

OUTCOME

The patient was recalled but had returned to Dubai to recover fully with her family. Both the patient and her local physician were contacted and she commenced treatment for neurobrucellosis with doxycycline, ceftriaxone and rifampicin. An echo was performed locally, but the results were not available to us. On direct questioning, the patient admitted to frequently consuming unpasteurised camel milk when in Dubai.

The infectious diseases team in the United Kingdom were able to obtain her old case notes, showing that during her first presentation to hospital with a second trimester miscarriage, her placental pathology showed acute chorioamnionitis and deciduitis. The placental tissue was examined by the local histopathology team who identified features in keeping with brucellosis. The patient's hospital admission with knee swelling was also reviewed – the aspirate was sent for RNA sequencing, and confirmed infection with *Brucellosis melitensis*.

Incidentally, the microbiology laboratory team involved in the case was seen by the hospital trust's occupational health department who determined that several staff members should commence post-exposure prophylaxis treatment with doxycycline.



CASE DISCUSSION

Brucellosis is the most common zoonotic infection in the world. Brucellosis can be transmitted from infected animals to humans via cutaneous, conjunctival or inhalation contact with infected matter. It can also be contracted by ingestion of meat and unpasteurised milk or cheese from infected animals. In this case, the patient admitted to regular consumption of unpasteurised camel milk, which is a known mode of brucellosis infection.

It can take weeks to months from the point of brucella infection until the onset of symptoms. Common features include fever, chills, fatigue and arthralgia. An acute monoarticular arthritis may develop. Brucellosis infection during pregnancy increases the risk of spontaneous miscarriage and fetal death.

This case highlights the importance of obtaining a thorough travel history – the patient had last visited an endemic area almost 1 year ago, but her various medical problems over the subsequent months can all be explained by a diagnosis of brucellosis.

With thanks to Dr Jon Lambourne for his assistance with this case.

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CASE 10: A RIGHT UPPER QUADRANT PAIN PUZZLE

PATIENT HISTORY

A 75-year-old woman presented to the emergency department complaining of abdominal pain. She had been feeling unwell for 3 days with fatigue, malaise, loss of appetite and right-sided abdominal pain. The pain was dull and constant in nature and graded at 4/10 in severity. It did not radiate and there were no clear exacerbating or relieving factors. She had been reviewed by her general practitioner (GP) 2 days earlier who had prescribed a course of trimethoprim for a presumed urinary tract infection. The patient denied any symptoms of dysuria or urinary frequency. Her bowels were open every 2–3 days with no diarrhoea and she did not feel nauseated. She had no other past medical history and took no regular medications. She had never smoked and did not drink alcohol. She lived alone and was independent for all activities of daily living.

EXAMINATION

Initial observations: T 37°C, HR 90 bpm, BP 130/75 mm Hg, RR 22, SpO₂ 97% on room air.

The patient was alert and orientated. She appeared comfortable at rest. She had an elevated body mass index, weighing approximately 150 kg. There were no signs of jaundice. Her chest was clear to auscultation and cardiovascular examination was unremarkable. Abdominal examination identified severe right-sided abdominal pain on light palpation. Palpation for organomegaly was not possible due to pain. Bowel sounds were normal. No rash or obvious swelling of the abdomen were observed.

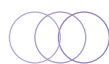
INITIAL RESULTS

Routine blood tests: WCC 7.8, Hb 137, Plt 178, Na 137, K 3.8, Creat 86, Bili 14, ALT 40, ALP 56, Amylase 30, INR 1.1, CRP 22.

DIFFERENTIAL DIAGNOSES

Hepatobiliary injury or infection would account for the symptoms of right upper quadrant pain, although typically you would expect deranged liver function tests. Possible diagnoses of acute hepatobiliary dysfunction include infectious or autoimmune hepatitis, cholecystitis, a portal or hepatic vein thrombosis or malignancy. Serum amylase is usually elevated in acute pancreatitis (more than 3 times the upper limit of normal) but may be normal or only slightly high in chronic or recurrent cases of acute pancreatitis, as the pancreas atrophies and fibroses, leading to a reduction in amylase production.

Appendicitis may present with generalised right-sided abdominal pain so it is important to ask the patient if she has previously undergone an appendicectomy and to look for a surgical scar. Constipation is a possible cause of her pain, particularly as the patient says that she opens her bowels every 2–3 days. Diverticulosis and diverticulitis are common conditions



in older patients and can be identified with a colonoscopy or computed tomography (CT) imaging.

The patient's GP suspected an underlying urinary tract infection. It is important to revisit why the GP diagnosed this. (Was there a positive urine dipstick test? Did the patient describe dysuria or urinary frequency at that time?) Her symptoms of pain and malaise could represent a urinary tract infection that has progressed to pyelonephritis.

A right-sided lower lobe pneumonia is another cause of right upper quadrant pain that can easily be missed. The patient denies symptoms of cough or shortness of breath but a chest x-ray is still indicated.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

A urine dipstick test must be performed to look for the presence of blood (suggestive of potential renal colic), leucocytes and nitrite (may be positive in urinary tract infection). The urine sample should be sent for culture if there are any features of infection on the urine dipstick or if the patient describes symptoms of urinary tract infection. The patient has already been treated with several days of antibiotics so a positive urine culture may not be obtained, although results may be available if a urine culture was sent by the GP.

The patient's abdomen is very tender – an erect chest x-ray should be requested to look for signs of a right basal pneumonia as well as potential air under the diaphragm (pneumoperitoneum), signifying abdominal visceral perforation. You should additionally request an abdominal x-ray as this may show signs of small and large bowel dilatation or bowel wall oedema.

Take a venous or arterial blood gas sample to evaluate the acid–base status of the patient and to check the patient's lactate level, which rises when tissue hypoperfusion occurs, as seen in sepsis.

If an abdominal ultrasound scan can be performed urgently, this should be arranged to image the kidneys, liver and biliary tract, although the patient may not tolerate this investigation due to her pain, in which case a CT scan of the abdomen may be required.

Prescribe analgesia, starting with paracetamol and escalating to opiates. She is currently haemodynamically stable and is not vomiting so there is no indication for intravenous fluids at present, provided the patient has a good urine output.

CASE PROGRESSION

The working diagnosis was pyelonephritis and the patient was commenced on broad-spectrum antibiotics. She became nauseated and intravenous fluids were therefore started. Her medical team prescribed regular paracetamol and codeine phosphate in addition to immediate-release morphine sulphate that was available on request.

The following day, the patient's urine sample showed no growth of bacterial organisms. The right-sided abdominal pain increased and she required large doses of morphine, which offered only minimal relief and induced nausea and vomiting. By the evening, she complained that the pain was now radiating through to her back. She remained haemodynamically stable and afebrile; she appeared well. Blood tests were repeated and showed no rise in inflammatory markers.

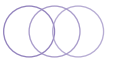


Figure 10.1 Erythematous, vesicular rash.

A CT scan of the aorta was performed to exclude an abdominal aortic aneurysm. This showed no abnormalities. The patient continued to complain of pain with little relief from opiate analgesia but remained clinically well. A surgical review took place and no obvious cause for her pain was identified.

On the morning of the second day, a rash developed over the right anterior T6-T7 distribution (see [Figure 10.1](#)). The rash was erythematous and vesicular and exquisitely tender to touch. Light palpation of the skin lesions reproduced her abdominal pain, with no other areas of tenderness around the abdomen. Swabs of the skin lesions were positive for varicella-zoster virus (VZV) DNA.

Diagnosis: Shingles in the T6-T7 distribution with pre-herpetic pain.

FINAL OUTCOME

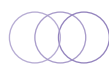
The patient was commenced on amitriptyline and her symptoms rapidly settled. She was discharged home for follow-up in the community.

CASE DISCUSSION

Initial exposure to VZV results in chickenpox. VZV can remain dormant in dorsal root ganglia and reactivate at a later stage of life leading to herpes zoster, also known as shingles. Vesicles form over an underlying area of erythema in a dermatomal distribution. Following the acute phase of the illness, symptoms of post-herpetic neuralgia with recurring episodes of pain around the affected dermatomes may develop.

Some patients, as in this case, will experience a period of pre-herpetic neuralgia. This is challenging to diagnose at the time of presentation. It is commonly the case that the diagnosis is made retrospectively, once the shingles skin lesions begin to develop.

Typical symptoms include a radicular pain that is severe and burning in nature. One or more dermatomes may be involved. Pre-herpetic neuralgia usually precedes the eruptive phase



by 2–3 days but can develop up to 10 days before the onset of skin lesions. Complications, including zoster encephalitis, can develop at this stage. Analgesia that specifically treats neuralgic pain, such as the GABA analogues, gabapentin and pregabalin, are often effective.

With thanks to Dr Fiona Perry for her help with this case.

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CASE 11: IT'S ALL IN YOUR HEAD

PATIENT HISTORY

A 29-year-old man was brought to hospital following a witnessed collapse at work. His colleagues described the patient collapsing to the floor followed by a 30-second period where all four limbs were jerking/shaking. There was a subsequent 5-minute period where he was unrousable and he then became progressively more alert over the next 15 minutes. The patient did not recall the events preceding his loss of consciousness. He had bitten his tongue and was incontinent of urine. He denied any previous episodes of collapse. He had no past medical history and took no regular medications. He worked at an estate agent company doing office work and lived alone. He had no sexual partners in the preceding year. He had never smoked and estimated that he drank around 20 units of alcohol per week. He denied recreational or herbal drug use. He was born in the United Kingdom and had lived there for all of his life. His last episode of travel had been a backpacking trip around Asia from which he had returned 6 months earlier.

EXAMINATION

Initial observations: T 36.8°C, HR 84 bpm, BP 126/80 mm Hg, RR 14, SpO₂ 99% on room air.

The patient was alert and fully orientated. He had some superficial lacerations and bruising over his left forearm and left shin. His chest was clear to auscultation and the heart sounds were normal. His abdomen was soft and non-tender, with no palpable organomegaly. A full neurological examination, including fundoscopy, identified no focal deficits.

INITIAL RESULTS

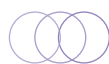
Routine blood tests: WCC 7.5, N° 4.3, L° 0.8, E° 2.1, Hb 132, Plt 306, Na 142, K 4.5, Creat 52, INR 1.0, CRP 4.

DIFFERENTIAL DIAGNOSES

Late-onset epilepsy is a possibility – although uncommon, people can present with a new diagnosis of epilepsy in adulthood. Epilepsy is diagnosed when a patient has experienced two or more episodes of seizures with no clear cause, at least 24 hours apart.

A space-occupying lesion is a relatively common cause of first adult seizures. Primary brain tumours, such as glioblastoma multiforme and central nervous system (CNS) lymphoma, or a secondary deposit from metastatic malignancy should be considered. A spontaneous intracerebral bleed can cause seizures and reduced consciousness, but the fact that the patient is now fully alert with no neurological deficits makes a large bleed unlikely.

Infections such as toxoplasmosis or a localised cerebral abscess may have developed, particularly if the patient has a history of immunosuppression. This patient is likely to have travelled to countries with endemic malaria. It is important to ascertain exactly where he has travelled



and when he visited the relevant country/countries to establish whether he is at risk of developing cerebral malaria.

Alcohol and recreational drugs are leading causes of seizures in adults, but this patient denies excessive alcohol consumption or any recreational drug use. Meningitis and encephalitis are also typically considered in first seizures, but this patient has no signs of infection, altered cognition or meningism.

We know that the patient has a normal sodium level, but tests should be performed to investigate for metabolic disturbances, such as hypocalcaemia and hypoglycaemia, which can lead to the development of seizures.

Syncope can be defined as a transient loss of consciousness and upright posture due to global cerebral ischaemia, and the underlying cerebral ischaemia can result in convulsive movements that are similar in nature to those seen in epileptic seizures. This patient had an estimated 10 minutes of being drowsy or unrousable following his collapse, which is not in keeping with syncope. An episode of cardiac arrhythmia can result in loss of cerebral perfusion, similar to syncope.

Last, non-epileptic seizure activity should be considered. These events, often prompted by psychological distress, can be easily mistaken for epileptic seizures.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

Blood tests should be sent to exclude hypoglycaemia and electrolyte disturbances. A magnetic resonance imaging (MRI) brain scan should be arranged to look for evidence of a space-occupying lesion, ischaemic changes associated with malaria, or abnormal signal intensity in the subfrontal and temporal regions associated with encephalitis. If an MRI brain scan cannot be performed immediately then a computed tomography (CT) head scan, ideally with contrast, should be scheduled urgently.

An EEG can differentiate between epileptiform and non-epileptiform activity, aiding the diagnosis of epilepsy versus psychogenic non-epileptic seizures.

CASE PROGRESSION

A CT head scan was performed at the time of admission. This showed a 9 mm ring-enhancing lesion on the left parietal lobe, likely to represent a neoplasm. Prophylactic levetiracetam was commenced, following neurology team advice, to prevent further seizures. An HIV test was taken – this came back negative.

An MRI brain scan was performed the next day – this showed a well-defined $13 \times 10 \times 10$ mm ring-enhancing lesion within the left parietal lobe with a 'dot-in-hole' appearance (see [Figure 11.1](#)), consistent with a diagnosis of neurocysticercosis. At this point, the infectious diseases team reviewed and elicited a full travel history. The patient had backpacked for 18 months in total, visiting India, Nepal, Vietnam, Thailand, Malaysia and Indonesia, returning 6 months prior to his admission to hospital. During this time he was staying in hostels and consuming street food. Serological testing confirmed a diagnosis of cysticercosis.

Final diagnosis: Seizure due to early degenerating neurocysticercosis lesion.

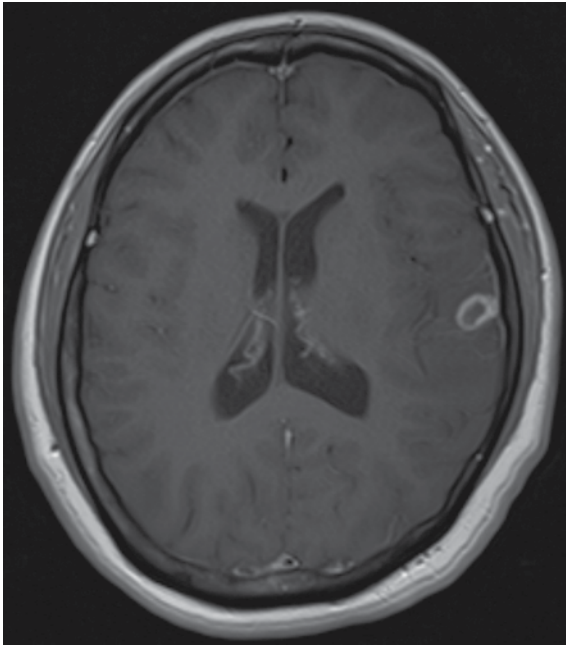
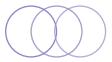


Figure 11.1 MRI brain scan showing a ring-enhancing lesion.

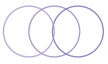
FINAL OUTCOME

The patient discussed treatment options with the team and decided to ‘watch and wait’, as the parasite would die (and the lesion would probably resolve) within a year. He was followed up as an outpatient where he described feeling panicked and suffering from headaches and elected to return to hospital as an inpatient to commence a course of anti-helminthic medication. He was prescribed 400 mg albendazole BD for 8 days, and 4 mg dexamethasone TDS starting 1 day pre-treatment, continuing through the course and then tapering afterward. He made a good recovery and serial neurological imaging is being performed at regular intervals.

CASE DISCUSSION

The differential diagnosis for a cerebral ring-enhancing lesion includes central nervous system (CNS) lymphoma and toxoplasmosis. These conditions are usually present in immunocompromised patients, hence the importance of an HIV test. Other causes of ring-enhancing lesions include a cerebral pyogenic abscess, tuberculomas, primary brain tumours (such as glioblastoma multiforme), metastatic malignant disease and neurocysticercosis.

Neurocysticercosis is the most common cause of acquired epilepsy and also the most common parasitic disease of the CNS in less economically developed countries. Cysticercosis is a *Taenia solium* (pork tapeworm) infection that is spread via a complicated cycle involving both pigs and humans. Pigs ingest tapeworm eggs in food and water that is contaminated with infected faeces. The eggs develop into cysticerci within the muscles of the pig and are subsequently consumed by humans eating raw or undercooked pork. The parasite attaches itself to the human intestinal wall, releasing ova into the gastrointestinal tract, which are



then excreted via the faeces and consumed by humans via contaminated food. The parasites hatch in their new host and travel into abdominal organs, as well as muscle, brain, ocular and subcutaneous tissues.

Typical treatment involves the administration of anti-helminthic agents, such as albendazole or praziquantel, although some clinicians opt to 'watch and wait' in patients with solitary brain lesions.

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CASE 12: HYPERPIGMENTED SKIN LESIONS

PATIENT HISTORY

A 35-year-old man presented to hospital complaining of a painful skin lesion on his left shoulder. The lesion had initially developed 3 months earlier but had become increasingly tender and inflamed. Green, malodorous fluid was now discharging from the lesion and the pain was not controlled with simple analgesia. In addition to the lesion on his shoulder, he reported similar lesions covering his limbs and trunk, which were painful and occasionally developed signs of infection. His past history was significant for an admission to hospital in Ghana 18 months ago, where he presented with fevers and vomiting and was treated for both malaria and typhoid. Following treatment with aminoglycoside antibiotics, he sustained an acute kidney injury requiring several weeks of haemodialysis and had since developed chronic kidney disease. He subsequently suffered from widespread bone pain, attributed to renal osteodystrophy. He often experienced fevers but denied night sweats or unintentional loss of weight. He took no medications currently and denied recreational or herbal drug use. He did not smoke or drink alcohol. He lived with his cousin and worked as a secretary. He had returned from Ghana 9 months earlier and had not travelled abroad since. He had multiple episodes of unprotected sexual intercourse with one female partner while in Ghana.

EXAMINATION

Initial observations: T 37.7°C, HR 98 bpm, BP 128/84 mm Hg, RR 14 and SpO₂ 99% on room air.

Of note, the patient had multiple black, necrotic lesions covering his body (see [Figure 12.1](#) of lower limb lesions; [Figure 12.2](#) for close-up view of a lesion). Some of the lesions were discharging pus. The largest lesion was over his left shoulder – this appeared to be a 6 × 7 cm abscess. Examination was otherwise unremarkable aside from a persistent low-grade fever and mild tachycardia.

INITIAL RESULTS

Routine blood tests: WCC 10.9, N^o 8.8, L^o 1.2, Hb 100, MCV 78, Plt 438, Na 138, K 4.0, Creat 132, CRP 82.

DIFFERENTIAL DIAGNOSES

HIV-related Kaposi's sarcoma is the most likely diagnosis at this stage. Infection with human herpesvirus 8 (HHV8) can lead to the development of spindle-cell tumours known as Kaposi's sarcoma, typically occurring in the presence of HIV infection. Cutaneous manifestations of Kaposi's sarcoma include hyperpigmented lesions, varying from violaceous to red-brown to black in colour. Lesions can appear over mucocutaneous areas or in a linear distribution over Langer's lines.

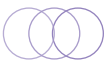


Figure 12.1 Lesions present on the lower limbs.

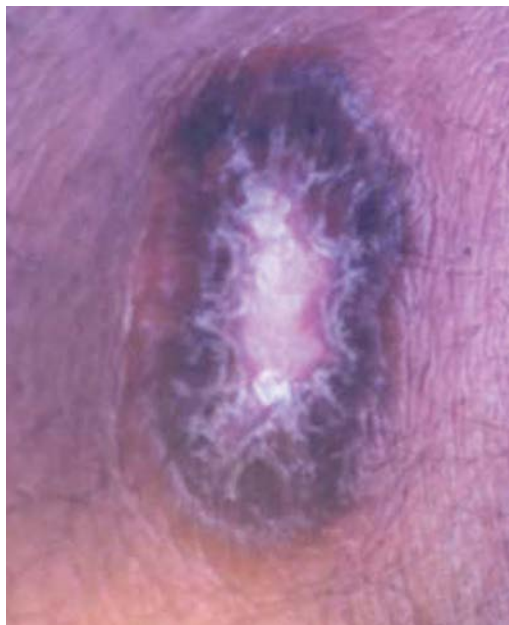
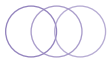


Figure 12.2 Close-up view of one of the skin lesions.



Cutaneous tuberculosis (TB) has several different forms, ranging from lupus vulgaris with reddish-brown nodules that are typically distributed over the face and neck, to scrofuloderma where lesions form over lymph nodes, joints and bones and can ulcerate over time. Cutaneous TB has a low incidence but is more common in patients co-infected with HIV.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient should be admitted for urgent medical and dermatology input. Blood cultures and swabs of the lesions should be sent. An HIV test should be performed. Despite a low-grade fever, he is haemodynamically stable and there is no indication to start antibiotics at present. If he develops features of sepsis then an antibiotic with activity against beta-lactamase-producing organisms, such as *Staphylococcus aureus*, should be considered.

The dermatology team should review this patient and obtain skin biopsies from the affected sites. Imaging of the bone(s) underlying the shoulder lesion should be obtained, starting with an x-ray, to look for evidence of osteomyelitis.

CASE PROGRESSION

The patient remained stable and antibiotics were not commenced. He had intermittent low-grade fevers ($<38^{\circ}\text{C}$) over the next few days. The dermatology team initially diagnosed probable Kaposi's sarcoma, but an HIV test was negative and skin biopsies showed large numbers of inflammatory cells with no malignant features. A full autoimmune screen was sent – this showed no abnormal results.

Swabs of pus from the shoulder lesion grew *Escherichia coli* and *Morganella morganii* bacteria, both of which were resistant to all antibiotics that the samples were tested for.

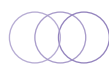
An x-ray of the shoulder had no features of osteomyelitis, but a subsequent magnetic resonance imaging (MRI) scan of the shoulder showed a large abscess, virtually replacing the deltoid muscle with possible humeral infarction. The abscess was incised and drained.

Several days into his hospital stay, it was elicited that the skin lesions had arisen predominantly in locations where the patient self-injected pentazocine subcutaneously while in Ghana. He had been using pentazocine for treatment of bony pain associated with renal osteodystrophy. He had not associated the skin lesions with the prior use of pentazocine until discussing his past history with the medical team. Subsequent dermatology review confirmed that these lesions were typical of pentazocine use.

Final diagnosis: Pentazocine-induced ulceration.

OUTCOME

The patient was discharged home and made a good recovery. His shoulder lesion healed well following debridement. He has areas of hyperpigmented scarring and nodules over many of the sites of pentazocine injection.



CASE DISCUSSION

Pentazocine is an opioid analgesic that is available in oral and injectable forms. It is rarely used in Western Europe, Australia and the United States but is more commonly prescribed in India and Western Africa for the treatment of moderate-to-severe pain. Pentazocine can be injected subcutaneously, intramuscularly and intravenously. Cutaneous complications of pentazocine injections are well-documented phenomena. Hyperpigmented lesions with ulceration at the sites of injection are a relatively common occurrence. Multiple case reports document the development of necrotic, ulcerating lesions that can lead to both local and systemic infection, as well as subsequent sinus and subcutaneous fibrous tissue formation.

This case highlights the importance of taking a thorough past medical and drug history from the patient. This patient did not connect his skin condition with previous pentazocine use as the lesions had developed gradually and were not seen at all sites of injection.

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CASE 13: LOSS OF VISION AND A MACULOPAPULAR RASH

PATIENT HISTORY

A 76-year-old man presented with sudden loss of vision in his right eye. On driving his car that morning, he was almost involved in a collision. At that point, he noticed loss of right-sided peripheral vision but was not aware of the precise time that his vision had deteriorated. There was no pain around the eye. Over the preceding week, he had experienced blurring of vision and floaters in his right eye. He denied further symptoms. His past medical history included hypertension and ischaemic heart disease. He took 5 mg amlodipine OD and 75 mg aspirin OD regularly. He lived with his husband but also had regular sexual intercourse with multiple partners. He stated that he always used barrier protection methods with all partners. A sexual health screen had been negative for HIV and syphilis 8 months earlier.

EXAMINATION

Initial observations: T 36.8°C, HR 60 bpm, BP 135/75 mm Hg, RR 20 and SpO₂ 99% on room air.

Abdominal examination identified mild right upper quadrant tenderness but no organomegaly. The patient had a maculopapular rash on the palms of his hands and soles of his feet, which he stated was longstanding. He had a right relative afferent pupillary defect. The visual acuity in the right eye was 6/18 (hand movements). Fundoscopy showed moderate haze in the right vitreous with a difficult fundal view. All other cranial nerves were intact and the patient had normal power, tone, reflexes, sensation and co-ordination in all four limbs.

INITIAL RESULTS

Routine blood tests: WCC 7.1, Hb 131, MCV 89, Plt 246, Na 131, K 5.7, Creat 78, Bili 14, ALT 84, ALP 538, GGT 527, INR 1.1.

DIFFERENTIAL DIAGNOSES

It is difficult to determine whether the patient's vision was truly lost suddenly, or if he only noticed this when driving. There are a limited number of conditions that lead to sudden visual loss, including central or branch retinal artery occlusion – this typically results in sudden and painless visual loss. Underlying causes include hypercoagulable states, diabetes mellitus, hypertension, hypercholesterolemia and atherosclerosis (particularly carotid atherosclerosis). Giant cell arteritis may also lead to central retinal occlusion. Amaurosis fugax may precede visual loss. On fundoscopy, the disc will appear swollen and pale.

Central or branch retinal vein occlusion can be differentiated from retinal artery occlusion through fundoscopy. The disc appears very swollen with sites of haemorrhage and cotton wool spots.

Optic neuritis can be a sudden or gradual onset in visual loss, typically preceded by pain. Patients may also notice a deterioration in colour vision (the colour red is particularly affected). Optic neuritis is strongly associated with multiple sclerosis.

Retinal detachment may be preceded by flashes of light, floaters and temporary blurring of vision prior to complete retinal detachment. The condition becomes more common with older age as the retina becomes thin and brittle. This patient describes similar symptoms.

Migraine may present with temporary visual loss, but patients usually have symptoms of a headache around the same time. It would be unusual for a first presentation of migraine to occur in an elderly patient.

Bacterial or fungal endophthalmitis is a bacterial infection that often occurs in the context of trauma or recent eye surgery. Patients tend to have a degree of underlying immunosuppression, e.g. poorly controlled diabetes, HIV infection, long-term immunosuppressive therapy, in the case of fungal endophthalmitis.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

This is an emergency and the priority is to prevent permanent visual loss. The patient will need urgent ophthalmology input and investigation. He will certainly require retinal imaging and possibly a vitreous biopsy.

Carotid imaging should also be considered, looking for vessel stenosis, either in the form of carotid Doppler studies or as a magnetic resonance angiography (MRA). The fact that multiple sclerosis is also being considered makes a magnetic resonance imaging (MRI)/MRA scan the preferred modality of imaging (as areas of demyelination are better seen using this test).

CASE PROGRESSION

The ophthalmology team reviewed the patient immediately and noted fine, keratic precipitates on the right cornea and 2+ cells in the anterior chamber. Fundal examination (see [Figure 13.1](#)) was obscured by significant vitritis and haze. There were white chorioretinal lesions and granular vitreal precipitates. The findings were consistent with right panuveitis with retinitis. The consultant reviewed and diagnosed acute retinal necrosis, possibly

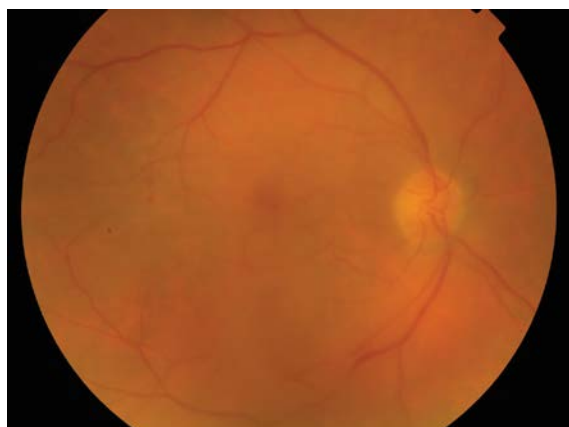
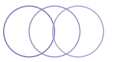


Figure 13.1 Fundus photograph.



secondary to varicella-zoster virus (VZV) or herpes simplex virus (HSV). The patient commenced intravenous aciclovir.

A vitreous biopsy was performed – polymerase chain reaction (PCR) was negative for Epstein–Barr virus (EBV), cytomegalovirus, HSV and VZV. An HIV test was negative.

A lumbar puncture was planned but not performed. Over the next 24–48 hours, the patient developed a maculopapular rash covering his limbs, abdomen and torso. This was initially thought to represent a drug reaction, possibly related to the aciclovir, but, as the rash progressed, the ophthalmology consultant advised that the rash was consistent with secondary syphilis. Blood tests were sent for syphilis serology and *Treponema pallidum* antibodies were detected (RPR titre of 1:32, consistent with active syphilis infection). The patient commenced intramuscular benzathine benzylpenicillin treatment.

Final diagnosis: Secondary syphilis resulting in pan-uveitis. The deranged liver function was attributed to syphilitic hepatitis.

OUTCOME

The patient has been followed up as an outpatient in the eye clinic. His vitritis has largely resolved and his retinitis is slightly better. His vision has remained at ‘hand movements’ in the right eye. His local genitourinary medicine clinic will follow up the patient and his husband.

CASE DISCUSSION

There are an estimated 12 million new infections of syphilis per year worldwide, making it one of the most common sexually transmitted infections. Secondary syphilis develops between 1 and 2 months after the primary infection and presents with a variety of features, including a rash, hepatitis, nephritis, arthritis, uveitis and retinitis. This patient had the classic rash seen in secondary syphilis, consisting of hyperpigmented macules beginning on the palms of the hands and soles of the feet and spreading to involve the trunk. Symptoms will usually resolve over 6 weeks. Early syphilis infection is usually effectively treated by a single intramuscular injection of benzylpenicillin. Azithromycin and doxycycline can be used as second-line agents.

The presence of syphilis infection enhances transmission of HIV. This is due to an increased risk of genital ulceration (and therefore mucosal damage) and the fact that *Treponema pallidum* induces the expression of a major co-receptor for HIV entry on monocytes. All patients testing positive for syphilis should be screened for HIV.

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CASE 14: CHEST PAIN AND AN ABNORMAL BLOOD FILM

PATIENT HISTORY

A 28-year-old woman presented to the emergency department complaining of a 4-day history of intermittent chest pain. The pain was central and crushing in nature and was present whenever she exerted herself. There was no associated shortness of breath or nausea and the pain did not radiate elsewhere. It was usually 4/10 in severity and settled with rest. On the most recent occasion the pain had been more severe and lasted for around 15 minutes. On direct questioning, she described menorrhagia over the previous week. Her periods were regular and she generally experienced light menstrual flow. Her past history included pulmonary tuberculosis 5 years earlier, which had been treated in South Africa. She took no regular medications. She worked as a sous chef and did not smoke or drink alcohol. She had one long-term sexual partner. She was originally from South Africa but had lived in the United Kingdom for the preceding 5 years.

EXAMINATION

Initial observations: T 37°C, HR 90 bpm, BP 120/70 mm Hg, RR 16, SpO₂ 99% on room air.

The patient was warm and well perfused. Her conjunctivae were pale. She had a regular heart rate of approximately 90 bpm. There was a soft ejection systolic murmur heard over the aortic area, which did not radiate and was thought to represent a flow murmur. There was no peripheral oedema. Her chest was clear to auscultation. Her abdomen was soft and non-tender with no palpable masses. There was no obvious bruising or rashes.

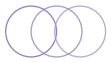
INITIAL RESULTS

Routine blood tests: WCC 8.5, Hb 64, MCV 90, Plt 20, Na 139, K 3.8, Creat 70, Bili 23, ALT 43, ALP 86, Alb 39, INR 1.0, APTT 1.0.

DIFFERENTIAL DIAGNOSES

This patient is experiencing exertional angina secondary to her low haemoglobin level. The thrombocytopenia may have led to menorrhagia, and subsequently, a drop in haemoglobin. If this is the case, the differential is as follows:

1. Decreased platelet production
 - a. Vitamin B₁₂ or folate deficiency. These conditions are rare in healthy, young people who adhere to a balanced diet. Vitamin B₁₂ deficiency may develop in patients with pernicious anaemia, although the patient has no known history of this.
 - b. Bone marrow infiltration, e.g. by military tuberculosis or myeloproliferative disorders. This patient has a past history of tuberculosis and bone marrow involvement is a possibility. She could also have metastatic disease with bone marrow



metastases. Examination of the breasts and lymph nodes should be performed to identify any signs suggestive of malignancy.

2. Increased platelet destruction
 - a. Thrombotic thrombocytopenic purpura (TTP) is an autoimmune condition that develops due to inhibition of the ADAMTS13 enzyme that breaks down von Willebrand factor. It usually manifests with symptoms and signs of renal impairment, microangiopathic haemolytic anaemia, thrombocytopenia, fluctuating neurology and fever.
 - b. Haemolytic uraemic syndrome (HUS) is a syndrome of thrombocytopenia and acute kidney injury, often in the context of recent gastrointestinal infection. *Escherichia coli* O157:H7 is a common causative agent. Children and young adults are typically affected. This patient has no signs of renal impairment or symptoms of diarrhoea or vomiting.
 - c. Idiopathic thrombocytopenic purpura (ITP) is an autoimmune condition where patients develop antibodies against platelet antigens. It is a diagnosis of exclusion (i.e. only diagnosed once other causes of thrombocytopenia are excluded).
 - d. Disseminated intravascular coagulation (DIC) is unlikely as the patient appears relatively well with no signs of shock, bruising or haemorrhage.
3. Drug-induced thrombocytopenia. Numerous drugs can cause thrombocytopenia, either by myelosuppression or accelerated platelet destruction, including gliclazide, thiazide diuretics, quinine, penicillins, ranitidine and several anti-epileptic drugs. The patient denies any regular medications, but she should be questioned in detail about medications that she may use occasionally, obtain from relatives or friends or buy over the counter.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

An urgent blood film should be obtained and the haematology doctor on-call should be made aware of the patient. As the patient is symptomatic from her anaemia, she is likely to require a blood transfusion, but before this is performed, blood samples should be taken for haematic investigations, including iron levels and iron binding studies, ferritin, and vitamin B₁₂ and folate levels. Blood should immediately be cross-matched so that the patient can have an urgent blood transfusion if she becomes haemodynamically unstable or develops further symptoms of cardiac ischaemia.

A chest x-ray (to look for hilar lymphadenopathy or an obvious lung malignancy) should be performed at admission.

CASE PROGRESSION

The patient remained stable overnight. She was initially due to receive a 2-unit packed red cell transfusion, but the haematology team reviewed the blood film and noted red cell fragments (schistocytes) consistent with a diagnosis of microangiopathic haemolytic anaemia (MAHA). Transfusion in the context of haemolytic anaemia is normally contraindicated as this may precipitate progression of the coagulopathy.

A routine HIV test came back as positive. On subsequent questioning, the patient explained that she was known to be HIV positive, taking antiretroviral therapy (Kaletra and efavirenz) but had not disclosed this as she had not thought that it was relevant to this presentation.



MAHA in the presence of normal coagulation is highly suggestive of TTP. Subsequent testing revealed reduced ADAMTS13 activity (<5%), and the presence of an IgG inhibitory antibody to ADAMTS13.

Final diagnosis: TTP, possibly secondary to HIV infection.

OUTCOME

The patient underwent plasma exchange with FFP and received intravenous high-dose steroids for 7 days and made a good recovery over the following weeks.

CASE DISCUSSION

TTP is a rare condition in which platelet thrombi form, leading to multi-organ damage. As red cells pass the intravascular clots, their membranes are damaged and the cells are broken into fragments. TTP may initially present with MAHA and thrombocytopenia. Untreated, the disease progresses to include symptoms, such as fluctuating neurology, fever and renal failure. TTP typically develops due to inhibition of the ADAMTS13 enzyme that breaks down von Willebrand factor.

There is mounting evidence that patients with HIV infection are at increased risk of developing TTP, possibly due to altered levels of von Willebrand factor production and the subsequent effect of this on ADAMTS13 activity.

In this case, the key to early diagnosis and treatment was involving the haematology team as soon as possible. Platelet transfusion in such cases can lead to worsening clinical symptoms, due to consumption of the transfused platelets and thus progression of microvascular thrombi formation. If there is significant bleeding or the need for an invasive procedure (e.g. central line insertion), a platelet transfusion should still be considered.

With thanks to Dr Michael Marks for his assistance with this case.

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CASE 15: A CONFUSED TRAVELLER

PATIENT HISTORY

A 61-year-old man presented to the emergency department complaining of a 2-week history of fevers, a dry cough and diarrhoea. He was experiencing episodes of shivering every 3–4 hours. The diarrhoea was described as watery brown stool with no blood or mucus. He had returned from Thailand 24 hours ago, where he had been for the preceding 4 weeks. He travelled to Thailand annually for holidays. On this occasion he had stayed in a hotel on the coast, had been eating street food and reported at least one episode of unprotected sexual intercourse with a female sex worker from Thailand. He had become intoxicated with alcohol and had fallen over in the street 3 weeks earlier, sustaining multiple lacerations to his legs. His past history included hypertension and peripheral vascular disease. He had received his UK childhood vaccine schedule with tetanus boosters, as well as immunisations for hepatitis A and typhoid immunisation prior to travel. He took an unspecified antihypertensive agent once daily. He worked as a pub landlord and was a current smoker with a 60 pack year history. He drank alcohol to excess but denied recreational drug use.

EXAMINATION

Initial observations: T 38.5°C, HR 105 bpm, BP 110/60 mm Hg, RR 18, SpO₂ 94% on FiO₂ 0.28.

The patient appeared to be mildly confused. His abbreviated mental test score was 8/10, losing points for recall and attention. Neurological examination identified left upper and lower limb dysmetria. There was no neck stiffness and he had no rash or eschar lesion. His chest was clear to auscultation. The heart sounds were normal with no murmurs. There were no signs of heart failure. His abdomen was tender throughout and there was a 1 cm liver edge palpable below the costal margin.

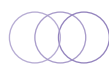
INITIAL RESULTS

Routine blood tests: WCC 12.5, N° 10.5, L° 1.4, Hb 119, MCV 94, Plt 131, Na 135, K 3.9, Urea 15, Creat 155, Bili 30, ALT 67, ALP 93, INR 1.2, CRP 302.

DIFFERENTIAL DIAGNOSES

The patient has a fever with cough, hypoxia and confusion. The presentation would be consistent with sepsis, possibly from sources such as meningococcal septicaemia and such possibilities must be considered.

Diarrhoea is a common feature of legionella pneumonia and this should be high up in the list of differential diagnoses, especially in view of his recent travel and time in a hotel. It would be helpful to ask him if the hotel was air conditioned but if not, legionella would still remain in the differential.



As he has travelled to Thailand and had unprotected sexual intercourse (UPSI) while there and on previous occasions it is critical that he is asked if he has had a test for HIV and that he is now tested for this and gonorrhoea and chlamydia. Disseminated gonococcus may present as septicaemia. *Pneumocystis jirovecii* pneumonia (PCP) should be considered, given the patient's symptoms of fevers and a dry cough that came on over several weeks. He is also more hypoxic than would be expected given his symptoms, which is in keeping with PCP.

He is a heavy smoker with a 60 pack year history and this should raise the possibility of pneumonia due to an underlying lung cancer.

Influenza is a common cause of cough, fever and malaise. Presentation may also include diarrhoea. It is unclear from the history above whether the patient has had an influenza vaccination this year, but in view of his travel history recently the possibility of influenza should be reviewed in the context of the current strains circulating, which may include strains not expected in the United Kingdom, such as an avian strain.

Typhoid fever is a possibility – the patient has a fever, diarrhoea and hepatomegaly. Patients with typhoid fever may develop bronchoconstriction and a dry cough is common, but typically those with typhoid are not significantly hypoxic. Rose spots and a relative bradycardia are well-known signs of typhoid fever, although these signs are commonly absent. Blood cultures are needed and the laboratory should be informed of the possibility of this and other tropical infections, such as *Burkholderia pseudomallei* (melioidosis) so any organisms can be handled appropriately.

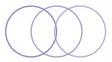
The majority of Thailand has a low risk of malaria, but certain rural areas along the borders of the country have a moderate risk of falciparum malaria. Patients with malaria may be confused and present in a similar way to this patient. They may develop a pneumonia or acute respiratory distress syndrome as well as a mild hepatomegaly.

Leptospirosis is spread via contact with animal (usually rodent) urine, particularly in areas without access to clean drinking water. This may initially present with a pneumonic illness, with fevers and shortness of breath as well as non-specific malaise. Confusion secondary to encephalitis and liver failure can also be features. The disease develops insidiously over several weeks.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

A computed tomography (CT) head scan must be performed in view of the patient's confusion and dysmetria. A full septic screen, including a chest x-ray, blood cultures and urine sample should be taken. Samples of the patient's diarrhoea should be sent for culture plus assessment of ova, cysts and parasites. Urine should additionally be checked for the presence of legionella antigen and leptospira polymerase chain reaction (PCR). Blood tests for HIV, syphilis, hepatitis, cytomegalovirus (CMV) and Epstein-Barr virus (EBV) serology should be sent, as well as three blood films to identify malaria parasites.

The patient has a dry cough making it difficult to send sputum samples for PCP analysis. A rapid HIV test should be performed to determine if this diagnosis is a possibility. If positive, an induced sputum sample can be obtained using nebulised hypertonic saline and the patient may require empiric treatment while awaiting results of testing.



His oxygen should be titrated to target oxygen saturations of greater than 94% initially. An arterial blood gas (ABG) sample should be taken to assess the degree and type of respiratory failure present and to allow adjustment of oxygen levels accordingly. In the context of sepsis, the lactate level from the ABG will also provide an immediate measure of anaerobic respiration due to tissue hypoperfusion, guiding your assessment of how unwell the patient is.

The patient is slightly hypotensive and tachycardic – an intravenous crystalloid fluid infusion, e.g. compound sodium lactate (Hartmann's solution) should be commenced, initially administering 2 L of crystalloids, with further intravenous fluids guided by the observations and urine output. To allow accurate fluid balance documentation, the patient should be catheterised, particularly as he is somewhat confused and may be unable to assist with recording his urine output.

Broad-spectrum antibiotics cover for a community-acquired pneumonia but also to include usual tropical infections such as typhoid and rickettsia. A suitable combination might therefore be ceftriaxone and doxycycline; however, if melioidosis is also possible then meropenem would be most appropriate. These choices would also safely cover the possibility of meningitis. If the HIV test is positive, commence treatment for suspected PCP.

CASE PROGRESSION

The patient commenced broad-spectrum antibiotics to treat a presumed pneumonia. He was also given aciclovir for treatment of possible encephalitis. A chest x-ray showed clear lung fields. A CT head scan was unremarkable. An HIV test was negative.

Over the next 48 hours the patient continued to spike high fevers and became increasingly confused. A magnetic resonance imaging (MRI) scan of the brain and lumbar puncture with cerebrospinal fluid (CSF) investigations were also unremarkable. His renal function improved and he maintained a good urine output with intravenous fluid support. At this point, the blood cultures taken at admission were growing gram-negative rods.

On the third day of admission, the patient's oxygen requirements rose and he developed dyspnoea. A repeat chest x-ray showed features consistent with acute respiratory distress syndrome. He was transferred to the intensive care unit and required intubation and assisted ventilation shortly afterward. Following review of the blood cultures, which were growing a *Pseudomonas*-type organism, the infectious diseases team advised that his antibiotics be switched from ceftriaxone to meropenem to cover for possible melioidosis. *Burkholderia pseudomallei* was subsequently isolated from the blood cultures.

Final diagnosis: Melioidosis.

OUTCOME

After a 3-week stay in the intensive care and high dependency units, the patient made a gradual recovery and was discharged home. He was re-admitted several days later with a hospital-acquired pneumonia but has since remained well.



CASE DISCUSSION

Melioidosis is endemic in parts of South East Asia, including Thailand, China and Malaysia. It is among the most common causes of sepsis in these countries (up to 20% in Thailand). The causative agent, *Burkholderia pseudomallei*, is a gram-negative saprophyte that is present in wet soil and rice paddy fields. The history from the patient should include exposure to such factors, such as working in rice-growing fields, and also whether the patient is diabetic, as this is a major risk factor for melioidosis.

The patient probably developed the infection following the fall 4 weeks earlier, where he sustained multiple wounds to his legs, allowing subsequent entry of the organism via this route. Melioidosis can be effectively treated with intravenous ceftazidime or carbapenems. In this case, the patient initially received ceftriaxone, a third-generation cephalosporin, which was ineffective against this particular infection.

With thanks to Dr Michael Marks for his assistance with this case.

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CASE 16: HEPATOSPLENOMEGALY

PATIENT HISTORY

A 26-year-old woman presented to the emergency department with nausea, diarrhoea, loss of appetite and general malaise. She could identify no clear precipitant to her gastrointestinal symptoms and denied having fevers or exposure to unwell contacts. Her symptoms had started approximately 10 days earlier and she was now feeling dehydrated. She also described developing peripheral oedema, beginning as mild ankle swelling a week ago, but now progressing to involve her shins. She had been treated for a lower respiratory tract infection with a course of amoxicillin 6 weeks ago but had been well for 4–5 weeks following this. The patient's past medical history included HIV diagnosed in childhood following vertical transmission (her HIV viral load was now undetectable, although her CD4 count remained low) with HIV-associated nephropathy and HIV-induced bone marrow suppression. She had been in good health over the preceding 18 months. She was taking 100 mg dapsone OD, 800 mg darunavir OD, 100 mg ritonavir OD and one tablet of Truvada (200 mg of emtricitabine and 300 mg of tenofovir) OD. She worked as a political journalist and lived alone. She had frequently travelled to rural areas of Spain over the past 2 years but had no other travel history. She occasionally smoked cigarettes (approximately five per week) and did not drink alcohol.

EXAMINATION

Initial observations: T 36.6°C, HR 105 bpm, BP 130/74 mm Hg, RR 18, SpO₂ 96% on room air.

The patient appeared clinically dehydrated with dry mucus membranes. Her jugular venous pressure (JVP) was elevated to the level of her ear lobe and she had pitting oedema to her abdomen. On auscultation of her chest there were bibasal crackles. Her abdomen was soft but distended and generally tender with normal bowel sounds. Mild hepatosplenomegaly was palpable.

INITIAL RESULTS

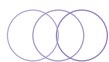
Routine blood tests: WCC 3.8, N^o 203, L^o 101, Hb 54, MCV 79, Plt 86, Na 130, K 6.7, Urea 24.8, Creat 301 (baseline 100), Bili 3, ALT 10, ALP 57, Alb 26, ESR 127, CRP 9.

Urine dip: 3+ protein and 4+ blood.

DIFFERENTIAL DIAGNOSES

The examination findings have identified gross oedema and the patient's urine dipstick test shows both haematuria and proteinuria, making an underlying glomerulonephritis likely. Glomerulonephritis is an immune-mediated inflammation of the glomerular tissues resulting in acute kidney injury.

Post-streptococcal glomerulonephritis (PSGN) is a possible diagnosis, particularly in view of the patient's recent respiratory tract infection. PSGN occurs 2–4 weeks following an infection with particular strains of group A β -haemolytic streptococcus.



Viral infections, including hepatitis (A, B and C), cytomegalovirus (CMV) and Epstein–Barr virus (EBV), can also cause an acute glomerulonephritis. Parasitic infections, including falciparum malaria, toxoplasmosis and trypanosomiasis are further causes, but the patient only lists Spain as a recently visited country.

Autoimmune conditions, including Goodpasture syndrome (GPS), where anti-glomerular basement membrane antibodies form, or systemic lupus erythematosus should be considered. GPS primarily affects the lungs and the kidneys, which could be causing the patient's symptoms of shortness of breath and cough over the preceding few weeks as well as her renal failure.

Many of the vasculitides, such as Henoch–Schönlein purpura and polyarteritis nodosa may precipitate renal failure with glomerulonephritis. Immunoglobulin A (IgA) nephropathy and membranoproliferative glomerulonephritis are other potential causes but would not explain the hepatosplenomegaly.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The most urgent problem is that the patient has severe hyperkalaemia. She should be treated immediately with 10% calcium gluconate, a dextrose and insulin infusion. Salbutamol nebulisers can also be considered as additional treatment. Either regular electrocardiograms (ECGs) or cardiac monitoring should be performed. The electrolytes and pH must be checked again once the infusion has run through.

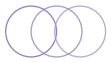
Assuming the hyperkalaemia has resolved, you should commence intravenous furosemide, either as a continuous infusion or as multiple boluses plus corticosteroid therapy. Close monitoring of renal function, electrolytes and blood pH will need to be performed. Insert a urinary catheter to allow accurate fluid balance. Send blood samples for an autoimmune screen plus anti-streptolysin O titre. Virology should be sent for hepatitis viruses, EBV and CMV.

Liaise with the renal team – this patient may require renal replacement therapy (RRT) (haemofiltration or haemodialysis), particularly if they become anuric or develop refractory acidosis or hyperkalaemia, or if their pulmonary oedema worsens. The renal team can also offer guidance as to the appropriateness of immunosuppressant therapy, such as cyclophosphamide.

Imaging of the abdominal organs is required – either as a computed tomography (CT) scan or an ultrasound scan. If a CT is performed, contrast would not be appropriate at this stage due to the underlying renal impairment. The patient also has moderate pulmonary oedema and may not be able to safely lie flat for a CT scan at this point in time.

CASE PROGRESSION

A renal ultrasound scan showed large, hyperechoic kidneys (right kidney 12.7 cm and left kidney 13.1 cm). Intravenous 40 mg furosemide BD was administered and the renal team advised commencing empirical steroids if the creatinine continued to rise. A renal biopsy was planned, but the patient's haemoglobin levels continued to fall and she became transfusion dependent over the subsequent days. Serum electrophoresis showed multiple bands in the γ region with polyclonal increase.



The patient's renal function remained stable and her oedema improved with diuretics. A CT scan of the chest, abdomen and pelvis was arranged to investigate for possible lymphoma. This showed hepatosplenomegaly (spleen 20 cm) and enlarged lymph nodes throughout the mesentery and retroperitoneum (largest nodes measuring approximately 2.6 cm). A positron emission tomography (PET) CT was subsequently performed, again showing widespread lymphadenopathy, interpreted as probable lymphoma.

An inguinal lymph node was biopsied. Rather than showing malignancy, this showed large numbers of what appeared to be Leishman–Donovan bodies, consistent with a diagnosis of leishmaniasis. Histoplasmosis could not be excluded as the parasites have a similar appearance and the infectious diseases team therefore advised sending blood tests for leishmania serology and histoplasmosis antigen and commencing a course of amphotericin B, which would treat both conditions. The leishmania direct agglutination test (DAT) test was positive (titre 1:102,400).

Final diagnosis: Visceral leishmaniasis (VL), acquired in Spain.

OUTCOME

The patient completed a course of amphotericin B followed by miltefosine. Her renal function recovered to baseline and she has now returned to work.

CASE DISCUSSION

VL is a protozoal infection that classically presents with fever, hepatosplenomegaly and bone marrow suppression. Sandflies are the vectors. It is important to think of this diagnosis in a patient with HIV from Spain, where VL is the third most common parasitic opportunistic infection after pneumocystosis and toxoplasmosis. VL co-infection increases the rate of HIV replication and disease progression while a low CD4 count affects the presentation of VL which can then be difficult to diagnose, as fever may be absent.

The treatment of choice is the anti-protozoal, amphotericin B. HIV infection significantly increases the risk of developing VL. This patient may have had a VL infection for several years, which may have been causing her bone marrow suppression, rather than HIV-related disease.

Renal impairment is a well-documented consequence of VL, due to immune complex disease leading to interstitial nephritis and proliferative glomerulonephritis.

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CASE 17: CUTANEOUS ULCERATION IN A PATIENT WITH RHEUMATOID ARTHRITIS

PATIENT HISTORY

A 69-year-old woman was referred to hospital by her general practitioner for assessment of painful lesions over her shins. The patient explained that she had suffered from lower limb venous ulceration for several years, but over the past 3–4 months she had noticed red patches on her shins, which were becoming increasingly inflamed and tender. She was now experiencing constant pain in her legs and her mobility was consequently becoming limited. She had been feeling short of breath for around 6 months and had experienced a dry cough for a similar duration of time. She had been referred to the chest clinic for investigation of her cough and was awaiting computed tomography (CT) imaging of her lungs. She reported unintentional weight loss of around 6 kg over 2 months. Her past medical history included hypertension, chronic obstructive pulmonary disease (COPD) and rheumatoid arthritis. She took regular 5 mg ramipril OD, 2.5 mg bisoprolol OD, 2.5 mg bendroflumethiazide OD, 20 mg methotrexate once weekly and 5 mg folic acid once weekly. She was a retired actress and lived with her husband and grandson. She was an ex-smoker with a 40 pack year history and drank around 10 units of alcohol per week.

EXAMINATION

Initial observations: T 36.5°C, HR 108 bpm, BP 102/60 mm Hg, RR 14, SpO₂ 96% on room air.

Examination revealed no abnormal signs in the cardiovascular, respiratory, abdominal and neurological systems. The patient was noted to have severe rheumatoid changes in her hands and feet bilaterally. There were multiple erythematous lesions covering her shins that ranged from 5 to 30 mm in diameter, some of which were nodular and some of which had a golden exudate and/or crusting (see [Figure 17.1](#)).

INITIAL RESULTS

Routine blood tests: WCC 12.4, N° 9.7, L° 2.5, Hb 8, MCV 84, Plt 385, Na 133, K 4.5, Creat 92, CRP 14, ESR 96.

DIFFERENTIAL DIAGNOSES

The patient has two main symptoms – cutaneous lesions and shortness of breath with a cough. She has a heavy smoking history and also describes recent weight loss in addition to her other problems. An underlying malignancy should be considered, particularly lung cancer. The skin lesions may represent a cutaneous paraneoplastic syndrome.

Cutaneous T-cell lymphomas, including both Sezary syndrome and mycosis fungoides, can present with erythematous, scaling maculopapular lesions.

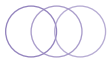


Figure 17.1 Lesions that were present over the patient's shins, some of which were nodular.

Pyoderma gangrenosum is a condition with deep, cutaneous ulceration. It typically affects the legs and is associated with underlying systemic conditions, including rheumatoid arthritis.

Behçet's disease classically begins with oral aphthous and genital ulceration. Uveitis is another common feature. As the disease progresses, lesions, similar in appearance to erythema nodosum, may develop over the lower limbs, along with acneiform lesions over the trunk.

Many of the vasculitides are associated with cutaneous lesions. Rheumatoid arthritis is associated with the development of cutaneous vasculitis.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient is hypotensive and tachycardic with no signs of peripheral or pulmonary oedema. She should be given intravenous fluid support, initially with a fluid challenge to see whether her blood pressure and heart rate improve. Her fluid balance will need to be monitored via strict input and output charts.

A chest x-ray should be performed in view of the history of shortness of breath and cough, particularly looking for any features of a lung malignancy, such as hilar lymphadenopathy or a lung mass. The lesions over the lower limbs should be swabbed for bacteria. If there are any particularly deep or necrotic ulcerations, an x-ray may be considered to look for signs of osteomyelitis.

An autoimmune and vasculitis screen should be sent and the dermatology team should be contacted for review of the lesions and to consider a skin biopsy.

CASE PROGRESSION

The tachycardia resolved and the patient's blood pressure rose to 122/80 mm Hg after intravenous fluid rehydration. A chest x-ray showed multiple nodular lesions throughout the lung fields.



She was noted to intermittently spike fevers of up to 38.4°C 2–3 times daily. Blood cultures were taken, but these showed no bacterial growth. The patient was re-examined and inguinal lymphadenopathy was identified, with large, firm nodes of up to 3–4 cm in diameter. On auscultation of her lungs she was noted to have bi-basal crackles.

She was reviewed by the dermatology team who identified oral ulceration, in addition to the cutaneous lesions, which they described as ‘a mixture of in-tact dome-shaped, ulcerated nodules and erosions, with crusting, not in any classical distribution’. A punch biopsy was taken. The main differential diagnosis at this point was cutaneous malignancy, such as non-Hodgkin’s lymphoma, with pulmonary metastases (cutaneous T-cell lymphoma). A CT scan of the chest, abdomen and pelvis showed multiple pulmonary lesions, likely to represent metastases, and hepatosplenomegaly. Bulky adrenals were also noted.

A bone marrow aspirate and trephine were taken. All histological samples were reviewed and were found to be consistent with a diagnosis of lymphoplasmacytic B-cell lymphoma (Waldenström’s macroglobulinaemia). Cells were positive for Epstein–Barr virus (EBV)-latent infection membrane protein-1. It was considered probable that the patient’s immunosuppression from methotrexate had led to active EBV infection and subsequent lymphoplasmacytic B-cell lymphoma.

Final diagnosis: Methotrexate-induced lymphoproliferative dysplastic disorder.

OUTCOME

The methotrexate was discontinued and no further treatment was commenced at this stage. The patient remained stable and her weight increased. A repeat CT scan of her chest performed 3 months later showed almost complete resolution of the lung nodules. She has remained well and is under surveillance in the community.

CASE DISCUSSION

Methotrexate-induced lymphoproliferative disorders are uncommon but well-documented in literature. Although often benign, physicians must be aware of this potentially serious complication, particularly as the disease may be reversible following methotrexate withdrawal.

Most cases of methotrexate-induced lymphoproliferative disorders are EBV related, probably secondary to the immunosuppression that the drug induces, even at the low doses used for treatment of rheumatoid arthritis.

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CASE 18: FIRST FIT

PATIENT HISTORY

A 30-year-old woman was brought to the emergency department after an episode of collapse while at home. Her sister witnessed the episode and described the patient suddenly collapsing to the floor followed by 5–10 minutes where her limbs were shaking. She had bitten her tongue and been incontinent of urine. The seizure self-terminated shortly before an ambulance arrived. She was drowsy for approximately 15 minutes after regaining consciousness. The patient seemed unable to vocalise on arrival to the emergency department and was communicating via gestures and nodding or shaking her head. She did not recall the event or post-ictal phase. She denied prodromal symptoms prior to her collapse. She had two identical episodes within the last fortnight, both of which left her unable to speak for several hours, followed by a period of speech disturbance. She denied any recent headaches, fevers or cough. She admitted to recent episodes of auditory hallucinations. She had no symptoms of pharyngitis, odynophagia, dysphagia or shortness of breath. She had no past medical or surgical history and had taken no regular or over-the-counter medications in recent months. Her parents and siblings were well. She lived with her sister and was an art student. She denied smoking or recreational drug use. She drank approximately 14 units of alcohol per week. She had one regular male sexual partner and used barrier contraception. She was born in the United Kingdom and travelled to Bangladesh every summer; she had returned from a trip to Bangladesh 6 weeks earlier.

EXAMINATION

Initial observations: T 36.4°C, HR 78 bpm, BP 120/84 mm Hg, RR 20, SpO₂ 98% on room air.

The patient appeared to be drowsy but orientated, although she was not vocalising. A full examination of cranial nerves II–XII revealed no abnormalities. She had normal tone, power, reflexes, sensation, co-ordination and proprioception in all limbs. There were no signs of cerebellar pathology. Her chest was clear to auscultation and her heart sounds were normal. Her abdomen was soft and non-tender. There was no palpable cervical, axillary or inguinal lymphadenopathy. The patient had no rash, neck stiffness or photophobia.

INITIAL RESULTS

Routine blood tests: WCC 5.5, N^o 2.2, L^o 2.5, Hb 130, Plt 260, Na 140, K 4.2, Creat 60, Bili 2, ALT 11, ALP 82, cCa 2.54, PO₄ 1.4, Mg 0.81, CRP 2, glucose 5.6.

Venous blood gas: pH 7.36, pCO₂ 6.41, lac 1.5, BE 0.5, HCO₃ 26.

Urine dipstick test: 2+ protein, 3+ blood, β-HCG negative (note the patient was menstruating).

DIFFERENTIAL DIAGNOSES

The patient presents with three recent episodes of tonic clonic seizures with no past history and no features of meningitis or recent illness. Although it is less common to



develop epilepsy as an adult, this is the most likely diagnosis given the lack of other symptoms.

Cerebral malaria is a possibility, given the fact that the patient has travelled to Bangladesh recently and was not taking malaria prophylaxis. This typically presents with headache, fever, impaired consciousness and seizures. The patient has been otherwise well recently, making this diagnosis less probable.

Tuberculous meningitis is another possibility, again based on the patient's travel history to Bangladesh. The diagnosis would be more likely if she had underlying HIV infection. The patient denies features of meningitis, such as headache, fever and photophobia.

A space-occupying lesion, such as a primary or secondary brain tumour can initially present with seizures. Other features include headaches, particular on waking, and nausea. Given the patient's age and sex, breast cancer would be one of the more common cancers to metastasise to the brain in this case.

Encephalitis is a further cause of seizures, but these usually develop at an advanced stage of the condition. A typical presentation is with headache, fever and altered mental state. The most common cause is herpes simplex virus (HSV) infection.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

In patients with a first episode of seizure, an urgent computed tomography (CT) head scan should be performed to exclude underlying haemorrhage, trauma or a space-occupying lesion. A capillary glucose level should be measured, as hypoglycaemia is a common and rapidly reversible cause of seizures. Patients should be screened for infection with a chest x-ray, urine dipstick test plus blood cultures, should they spike a temperature. History taking should specifically focus on any alcohol or recreational drug use – alcohol withdrawal can precipitate seizures.

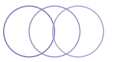
Cardiac arrhythmias, such as ventricular tachycardia, can lead to seizures. An electrocardiogram (ECG) should be performed, looking particularly at the QTc interval, and for evidence of heart block. A 24-hour tape should be considered.

Electrolytes, including sodium, potassium, magnesium and calcium, should be checked. In this case, they are all within the normal range. An anti-epileptic drug, such as levetiracetam, will be commenced as per local neurology guidance.

The patient needs to be observed for at least 24 hours and if she remains free of further seizures, she should have neurology follow-up arranged with a magnetic resonance imaging (MRI) scan of her brain. If she continues to have further seizures, an electroencephalogram (EEG) should be performed and a second anti-epileptic agent may be considered.

CASE PROGRESSION

The patient was admitted for a period of monitoring. She began communicating with single words rather than using sentences. She remained intermittently drowsy but was easily roused. A non-contrast CT head scan showed no abnormalities. She was admitted under the medical team



and was reviewed by the neurologists who noted that she had diminished reflexes throughout but no other abnormal signs. The working diagnosis at this stage was that of adult-onset epilepsy.

The following morning, the patient was drowsier and less communicative. She obeyed commands but was withdrawn, making poor eye contact. Her blood results remained stable and she had not had any febrile episodes. Three blood films showed no malaria parasites. An HIV test was negative.

Later that day, the patient became confused and was acting inappropriately, taking other patients' notes and pacing up and down the ward in an agitated state. Intravenous aciclovir was commenced to cover for possible viral encephalitis. A lumbar puncture was performed with mild sedation using a benzodiazepine (2 mg lorazepam). An opening pressure was not recorded due to the patient's agitation during the procedure. Samples were sent for microscopy and culture, cell count, protein levels, viral screening and acid-fast bacilli. Spare samples were taken for further testing if required.

Lumbar puncture results showed no white cells, minimal red cells and a normal protein level. Gram stain was negative for organisms and there were no acid-fast bacilli on the smear.

A non-contrast MRI scan that evening showed small white matter lesions that were unlikely to be of significance, but an MRI scan with contrast was recommended when the patient was less agitated (due to movement artefact). The infectious diseases team reviewed and advised that an infectious cause of the patient's condition was unlikely. An underlying functional cause was considered. The spare cerebrospinal fluid (CSF) samples were sent for *N*-methyl-D-aspartic acid (NMDA) receptor antibodies and voltage-gated potassium channel antibodies.

The neurological examination was repeated the next day. The team noted that the patient did not respond to finger movements during visual field assessment but could count fingers in all areas. During the sensory examination, it became apparent that the patient was responding with 'no', to all questions.

An EEG was severely abnormal with bilateral independent bursts and arrhythmic runs of high-voltage sharpened delta activity over the frontotemporal areas on both sides. These abnormalities were more prominent on the left, perhaps in keeping with her speech impairment. There was no seizure activity. The findings indicated a severe bilateral encephalopathic process, with clear frontotemporal accentuation and left preponderance.

The fluctuation in her condition was felt to possibly represent episodes of non-convulsive seizures and she was commenced on 250 mg levetiracetam BD and the aciclovir was continued. The viral screen performed on her CSF samples was negative for HSV, varicella-zoster virus (VZV), enterovirus and parechovirus.

Over the following days, the patient remained intermittently drowsy with episodes of agitation. She was easily distracted and often mute for hours at a time. Two repeat EEGs showed some mild improvement but were still highly abnormal. Aciclovir was continued and the dose of levetiracetam was increased. The neurology team advised commencing intravenous immunoglobulin (IVIg) and high-dose corticosteroid therapy (50 mg prednisolone OD) for the treatment of possible autoimmune encephalitis.

Due to her high levels of agitation, the patient was electively intubated and ventilated to facilitate further management. The patient showed no improvement following IVIg therapy. A consultant neurologist advised that adult patients with anti-NMDA receptor encephalitis tend to show minimal response to immunosuppression therapy and that plasma exchange should be commenced as the next step. Again, the patient did not improve. Rituximab was commenced and the patient



improved significantly. She quickly began to verbalise coherently and was soon able to communicate normally. CSF results subsequently confirmed the presence of NMDA receptor antibodies.

Final diagnosis: Anti-NMDA receptor encephalitis.

OUTCOME

The patient underwent a period of inpatient rehabilitation, including time spent with the neuropsychiatry team. An MRI scan of her pelvis was performed to exclude an underlying ovarian teratoma – this was unremarkable. She was discharged home several weeks later and has now returned to her studies. She has been advised to avoid leaving the United Kingdom for the next year due to her immunosuppression.

CASE DISCUSSION

NMDA receptors are a class of glutamate receptors that are responsible for processes involved in memory function, synaptic plasticity and generation of rhythms involved in breathing and locomotion. Anti-NMDA receptor encephalitis is a form of autoimmune encephalitis where patients develop antibodies to the NR-1 subunit of the NMDA receptor.

This is a progressive, multistage condition typically presenting with anxiety or withdrawn mood, progressing to psychiatric symptoms of auditory or visual hallucinations and/or paranoid thoughts. Patients subsequently develop memory loss, followed by seizures, dyskinesias, a reduced conscious level and, ultimately, death from respiratory or autonomic failure. This patient had many of these features but presented initially with seizures and psychiatric symptoms.

Anti-NMDA receptor encephalitis affects females in 80% of cases and is more prevalent in teenagers and young adults. In around 50% of cases in female patients, there is an associated malignancy, typically an ovarian teratoma. This patient had an MRI scan of her pelvis, which showed no abnormal masses.

It is important to consider autoimmune encephalitis in patients presenting with psychiatric symptoms. The condition is potentially reversible with immunosuppression and patients often have a good outcome, returning to near baseline function.

With thanks to Dr Yin Wu for his help with this case.

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CASE 19: A PLEURAL EFFUSION ON A BACKGROUND OF KNEE PAIN

PATIENT HISTORY

A 51-year-old woman presented to the emergency department complaining of shortness of breath. She described suddenly becoming aware of mild shortness of breath 1 week earlier and this had now progressed to the point where she was dyspnoeic on minimal exertion. She had a non-productive cough which had been present for 24 hours. She denied any recent fevers, night sweats or weight loss. She also had a 12-hour history of constant, dull, right-sided chest pain, which was exacerbated by lying flat. She had no recent surgery or episodes of prolonged immobility. Her past history included bilateral osteoarthritis of the knees, for which she had recently been referred to the rheumatology department, and type 2 diabetes mellitus. She took regular 500 mg metformin BD and occasional paracetamol for knee pain. She lived with her husband and worked as a special needs teaching assistant. Neither she nor her husband had ever smoked. She had not travelled abroad in recent years.

EXAMINATION

Initial observations: T 37°C, HR 88 bpm, BP 124/90 mm Hg, RR 16 and SpO₂ 95% on room air.

The patient was alert and orientated. She spoke in full sentences but did appear breathless at rest. There were absent breath sounds at the right base, which was also dull to percussion. The left lung sounded clear. Her heart sounds were normal, her jugular venous pressure (JVP) was not elevated and she had mild ankle oedema. Her abdomen was soft and non-tender.

INITIAL RESULTS

Routine blood tests: WCC: 10.7, N^o 7.1, L^o 2.2, Hb 108, MCV 87, Plt 428, Na 136, J 5.2, Creat 86, Bili 12, ALT 11, ALP 396, Alb 37, CRP 46.

DIFFERENTIAL DIAGNOSES

The patient has a unilateral pleural effusion with ipsilateral chest pain and was apparently fit and well until 1 week earlier. The first diagnosis to consider is a community-acquired pneumonia with a parapneumonic effusion. This would fit with the relatively rapid onset of her symptoms, the recent history of a cough, the elevated C-reactive protein (CRP) level and the mildly elevated neutrophil count.

A primary lung tumour is one of the more common causes of a unilateral pleural effusion, although it may be somewhat less likely in this case where the patient has no smoking history. She could have a primary cancer elsewhere, e.g. a breast cancer, with pulmonary deposits. Mesothelioma often presents with a pleural effusion – a full occupational history from both the patient and her husband should be obtained to assess the risk of asbestos exposure. This



is particularly important when considering a pleural aspiration or chest drain insertion, as needle-track malignant seeding is known to occur with this cancer.

A pulmonary embolism (PE) should be high up in the list of differential diagnoses. The patient gives a history of chest pain, albeit non-pleuritic in nature, and has a pleural effusion, both of which could be attributed to a PE. Pulmonary ischaemia and infarction will drive an inflammatory response that generates increased levels of interstitial fluid. Another possibility is that the patient has a primary or secondary cancer that has led to the development of a pleural effusion, and the associated hypercoagulable state has driven PE formation.

Heart failure is a possible cause of pleural effusions, but these tend to be bilateral rather than unilateral. When unilateral effusions do develop in the context of congestive cardiac failure, they are typically on the right side, rather than the left. The mechanism underlying this is unclear.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient is haemodynamically stable and afebrile at present with no definite diagnosis of pneumonia. It would be reasonable to hold off prescribing antibiotics at this stage until we have further information about the nature of the condition. If the patient develops a fever, tachycardia or hypotension then this should be reviewed. A breast examination should be performed to identify any large breast lumps that may represent an underlying malignancy.

A chest x-ray should be requested to confirm the presence of a pleural effusion, evaluate the apparent size of the effusion and establish whether there are any masses or if the hilar lymph nodes appear enlarged, supporting a diagnosis of malignancy. Further imaging will ultimately need to be obtained, with a computed tomography (CT) scan of at least the chest, if not the abdomen and pelvis as cancer staging. If the pleural effusion is large, the respiratory team may prefer to drain this prior to the CT scan of the chest to allow clearer views of the pleura.

CASE PROGRESSION

A chest x-ray showed a right-sided pleural effusion ([Figure 19.1](#)). The patient was admitted under the medical team for further management. No antibiotics were started at this point.

The respiratory team reviewed the patient the next day and did an ultrasound scan of the right lung, followed by an ultrasound-guided chest drain insertion and pleural biopsy. The plan was to drain the pleural effusion and to then perform a CT scan (with contrast) of the chest, abdomen and pelvis to investigate for possible malignancy with lung involvement.

Around 400 mL blood-stained fluid with clots was drained from the right pleural cavity. The patient initially felt more comfortable and was able to mobilise without dyspnoea. She became increasingly short of breath over the subsequent 2 days and on the third day of admission, she desaturated to 82% on room air, requiring FiO₂ 28% to maintain saturations of greater than 94%.

A CT pulmonary angiogram (CTPA) showed no evidence of pulmonary embolism but did demonstrate multiple nodular soft tissue opacities throughout both lungs. The largest was

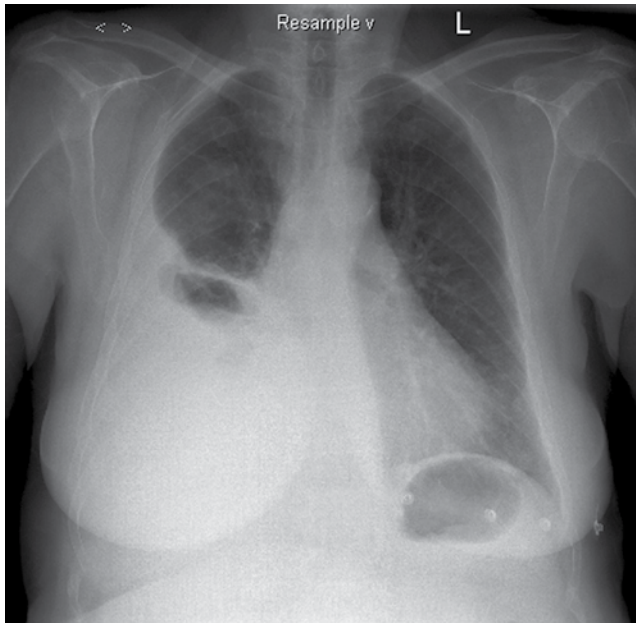
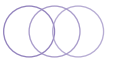


Figure 19.1 Chest x-ray showing a large right-sided pleural effusion.

seen in the right upper lobe and measured 25 mm × 24 mm. A large right-sided pleural effusion remained with associated consolidation/collapse of the right lower lobe. There was an impression of focal areas of enhancement within the right lower pleura, likely to represent pleural deposits. There was no evidence of pleural calcification and no enlarged mediastinal or hilar lymph nodes.

The following day, she spiked a fever of 38°C and complained of pain and swelling around her left knee. On examination, the knee appeared erythematous, swollen and hot to touch. There was a moderate-sized effusion around the joint. There was no swelling or erythema of the calf or thigh. The on-call physician aspirated serous fluid from the left knee using a needle and syringe. A knee x-ray was subsequently performed, showing a large mass within the femur infiltrating the surrounding soft tissues ([Figure 19.2](#)).

At this stage, the histopathology results became available from the pleural biopsy. The tissue sample showed a malignant neoplasm with sarcomatoid morphology. Samples from the lesion within the femur also confirmed this.

Final diagnosis: Primary osteosarcoma with lung metastases.

OUTCOME

The patient was referred to a specialist unit for further treatment. A combination of radiotherapy and chemotherapy was commenced.



Figure 19.2 X-ray showing a mass within the femur infiltrating the surrounding soft tissue.

CASE DISCUSSION

Osteosarcoma is a primary bone malignancy that typically affects teenagers and young adults. Risk factors for developing the disease as a younger adult include Paget's disease and exposure to radiotherapy. The cancer usually develops at the end of long bones, with the distal end of the femur and the proximal end of the tibia being among the most frequent sites of occurrence.

The disease can progress rapidly and may metastasise to the lungs or lymph nodes. Treatment options include surgery, chemotherapy and radiotherapy depending on the progression and prognosis of the disease.

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CASE 20: CHEST PAIN WITH A GYNAECOLOGICAL CAUSE

PATIENT HISTORY

A 27-year-old woman presented to the emergency department complaining of central chest pain and feeling light-headed. The pain came on gradually around 36 hours ago and had become severe over the past 12 hours. It was a tearing pain that radiated down to the patient's upper abdomen and was worsened by deep inspiration. She denied nausea, vomiting or diaphoresis. She stated that she had been well recently, with no symptoms of fever or cough. Her past medical history included hay fever and eczema. She took no regular medications. She smoked 20 cigarettes daily but denied regular alcohol intake or recreational drug use. She worked as a historian and had not travelled abroad for more than 2 years.

EXAMINATION

Initial observations: T 37.2°C, HR 82 bpm, BP 110/60 mm Hg, RR 16 and SpO₂ 98% on room air.

The patient was alert and orientated. Her chest was clear to auscultation. Her heart sounds were normal, her jugular venous pressure (JVP) was not elevated and she had no peripheral oedema. Her calves were soft and non-tender. The chest pain was reproducible on palpation of the lower half of her anterior chest wall bilaterally. Her abdomen was soft, but she had right upper quadrant pain on deep palpation. Her bowel sounds were normal. She was not icteric. A neurological examination was not performed.

INITIAL RESULTS

Routine blood tests: WCC 15.9, N^o 13.8, L^o 1.9, Hb 121, MCV 80, Plt 299, Na 128, K 3.8, Creat 58, CRP 43, TnT <3.

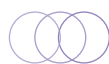
Urine dipstick test: No abnormalities detected; β -HCG negative.

Electrocardiogram (ECG): normal sinus rhythm.

DIFFERENTIAL DIAGNOSES

An acute coronary syndrome is unlikely. Aside from smoking cigarettes, the patient has no risk factors for cardiac disease. Her troponin T level, taken 12 hours after the pain peaked, was not elevated, serving to further reassure that there is no evidence of myocardial infarction.

The tearing nature of the pain should prompt consideration of aortic dissection. Acute aortic dissection is typically associated with sudden-onset pain that may radiate to the back. Again, the patient has no known risk factors for this condition, such as a connective tissue disorder, hypertension or Turner's syndrome.



The pain is worse on deep inspiration, suggestive of a possible pulmonary embolism (PE). There was no clinical evidence of deep vein thrombosis in the calves. Pain from pulmonary emboli can come on suddenly shortly after the clot occurs, or can develop gradually as pulmonary inflammation worsens. A right-sided pneumonia may present with right upper quadrant pain.

The fact that the patient has pain on palpation of the right upper quadrant means that diagnoses of pancreatitis, cholecystitis and an acute liver injury should be considered. The initial results do not include liver function tests or an amylase level to further guide the diagnosis.

HOW WOULD YOU MANAGE THE PATIENT ACUTELY?

Analgesia should be prescribed, starting with paracetamol and ibuprofen and escalating to weak opiates if needed. A chest x-ray will be useful in this case, potentially showing evidence of a pneumonia or other lung pathology such as a small pneumothorax. A widened mediastinum may be suggestive of an aortic dissection. In view of the elevated inflammatory markers, you may consider commencing broad-spectrum antibiotics to cover a pneumonia and a possible abdominal source of infection. Further blood tests, such as liver function tests and a clotting screen, should be sent as well as blood cultures if the patient develops a fever. An HIV test should be performed.

Depending on the chest x-ray findings, further imaging may be required. A ventilation/perfusion (V/Q) scan or a CT pulmonary angiogram (CTPA) should be considered, to look for evidence of pulmonary emboli, if there are no signs of pneumonia on the chest x-ray. A CTPA involves a higher dose of radiation exposure compared with a V/Q scan and therefore would only be performed if the test was needed urgently or if the patient had an abnormal chest x-ray or pulmonary disease that would be expected to cause a ventilation/perfusion mismatch. If the right upper quadrant pain persists or the patient has deranged liver function then an ultrasound scan of the abdomen is warranted.

CASE PROGRESSION

The chest x-ray showed no consolidation and the mediastinum appeared normal. The patient had a V/Q scan that showed no evidence of a PE. Her liver function blood tests showed elevated transaminase levels. She was treated with co-amoxiclav for a presumed lower respiratory tract infection.

Her chest and upper abdominal pain worsened throughout the day, requiring strong opiate analgesia. The pain remained worse on deep inspiration and was now radiating down to her legs. A CT scan of the aorta was performed to exclude aortic dissection. This showed a normal appearance of the aorta but also found bilateral complex adnexal cystic lesions measuring up to 5.5 cm in size seen above the fundus of the uterus and with adhesions to the adjacent small bowel loops (see [Figure 20.1](#)). There was free fluid around the liver capsule with fat stranding in the lower abdomen.

The following day, the patient was found to have abdominal guarding and was reviewed by both the gynaecology and surgical teams. A transvaginal ultrasound scan was recommended, but the patient declined this. The gynaecology team arranged a laparoscopy and later proceeded to a laparotomy. They performed a left salpingo-oophorectomy. Histology

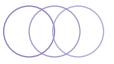


Figure 20.1 CT scan showing bilateral complex adnexal cystic lesions.

showed both acute and chronic suppurative salpingo-oophoritis with abscess formation (pelvic inflammatory disease, PID). Culture of pus obtained during the surgery grew *Chlamydia trachomatis*. Clarithromycin was commenced.

Final diagnosis: PID secondary to *Chlamydia trachomatis* infection with inflammation of the liver capsule (Fitz-Hugh–Curtis syndrome).

OUTCOME

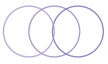
The patient later developed sepsis and underwent a further laparotomy and wash-out with a right salpingectomy. She was discharged home with gynaecology follow-up.

CASE DISCUSSION

Fitz-Hugh–Curtis syndrome is a complication of PID, where patients develop inflammation of the liver capsule secondary to the spread of a genital infection, typically *Chlamydia trachomatis* or *Neisseria gonorrhoeae*. The infection can spread directly or via the haematogenous or lymphatic routes.

Patients present with right upper quadrant pain along with signs of salpingitis. The pain may worsen on coughing or deep inspiration due to inflammation around the liver or diaphragm. Often, the pain radiates to the right shoulder tip, although not in this case. Fitz-Hugh–Curtis is an important diagnosis to consider in women presenting with right upper quadrant pain. The incidence of Fitz-Hugh–Curtis syndrome in women with PID is thought to vary from 5% to 15%.

This case highlights the importance of taking a sexual history and performing a sexual health screen where appropriate. It also emphasises the importance of considering alternative diagnoses in patients presenting with chest pain, particularly when they lack features



of common diagnoses such as lower respiratory tract infections, gastro-oesophageal reflux disease or cardiac ischaemia.

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CASE 21: ITP OR NOT ITP?

PATIENT HISTORY

A 16-year-old Caucasian woman presented to the emergency department complaining of abdominal pain and vomiting. She described a 4-day history of coffee ground vomiting 3–4 times daily. Over the last day, she had developed severe abdominal pain radiating from the loin to the groin on the right side. Her past history included idiopathic thrombocytopenic purpura (ITP) diagnosed when she was 4 years of age, menorrhagia, several presentations with renal colic in the past 5 years, migraines associated with menstruation and longstanding intermittent haematuria. On direct questioning, the patient described multiple episodes of haematemesis occurring every few months since she was approximately 12 years of age. She took no regular medications. There were no known familial illnesses. She lived with her parents and was in full-time education. She denied smoking or alcohol intake.

EXAMINATION

Initial observations: T 35.4°C, HR 65 bpm, BP 122/88 mm Hg, RR 18 and SpO₂ 100% on room air.

The patient was alert and orientated. She had pale conjunctivae and dry mucus membranes. Her chest was clear to auscultation. Her heart sounds were normal and there was no peripheral oedema. Her abdomen was soft with normal-pitched bowel sounds. She had tenderness on palpation around the left flank. Digital rectal examination was not performed.

INITIAL RESULTS

Routine blood tests: WCC 6.8, Hb 135, Plt 79, Na 139, K 4.1, Creat 86, INR 1.0, CRP 1.

Urine dipstick test: large blood clots present. The patient was not currently menstruating.

DIFFERENTIAL DIAGNOSES

Assuming the patient's diagnosis of ITP is correct, it seems likely that she has had a recurrence of her longstanding renal colic. Given her history of abnormal clotting function and large blood clots present in her urine, it may be the case that blood clots are causing her renal colic. Pyelonephritis is unlikely as the patient denies urinary frequency or dysuria and her inflammatory markers are not elevated.

Her haematemesis may be explained by a Mallory–Weiss tear following multiple episodes of vomiting. Alternatively, she may have an underlying gastritis, oesophagitis or peptic ulcer disease.

It would be very useful to have further information about how the diagnosis of ITP came to be made. If the diagnosis of ITP is incorrect, other potential bleeding disorders should be considered. If this is the case, the low platelet count could be attributed to large volume bleeding.

Hereditary haemorrhagic telangiectasia (HHT) is a condition where vascular malformations can cause cutaneous and gastrointestinal bleeding.

Von Willebrand disease (vWD) is another possibility – this is the most common hereditary bleeding disorder and occurs due to a deficiency in von Willebrand factor, a glycoprotein that mediates platelet adhesion and also binds clotting factor VIII.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient describes ongoing upper gastrointestinal bleeding and, although currently haemodynamically stable, she is at risk of major haemorrhage. She should have bilateral large-bore cannulae sited in her antecubital fossae. Blood samples should be sent for ‘group and save’ (to determine the patient’s blood group and whether any antibodies to red cell antigens are present). If the patient develops hypotension or tachycardia then blood would need to be urgently cross-matched.

A blood film should be reviewed to look at the appearance of the platelets and to identify any obvious abnormalities. She will need formal clotting studies and her condition should be discussed with the haematology team.

The patient should be given analgesia and anti-emetics. An oesophago-gastro-duodenoscopy (OGD) should be scheduled to look for points of recent bleeding or ulceration within the upper gastrointestinal tract. She will need to be kept ‘nil-by-mouth’ until the OGD has identified the bleeding point. Intravenous fluids should be prescribed. A computed tomography (CT) scan of the renal and urinary tract can also be arranged to look for an obstructive lesion.

CASE PROGRESSION

The patient was kept ‘nil-by-mouth’ and an urgent OGD was performed. This showed no bleeding points. A biopsy of the gastric mucosa tested negative for the presence of *Campylobacter*-like organisms (*Helicobacter pylori*, HBP).

The CT scan of her renal and urinary tract showed no calculi.

A blood film showed thrombocytopenia with large platelets (see [Figure 21.1](#)). A von Willebrand screen was unremarkable. There was no fall in the haemoglobin level when this was re-checked 24 hours later. The patient was unsure whether she was definitely experiencing haematemesis rather than haemoptysis. A flexible nasendoscopy found no evidence of bleeding. A CT chest scan was performed, to investigate for structural causes of haemoptysis, but there were no pulmonary emboli or arteriovenous malformations seen.

Stool samples were positive for HBP antigen. Eradication therapy was commenced on haematology advice, as HBP infection is a known well-documented cause of thrombocytopenia. The patient was discharged home for further investigations in the community. She re-presented to hospital several weeks later with haematuria. She was given human leucocyte antigen (HLA)-matched platelets during a cystoscopy but had a transfusion reaction to these, requiring treatment with adrenaline, chlorpheniramine and hydrocortisone.

Subsequent platelet studies showed markedly reduced aggregation with ristocetin and a near normal aggregation with other agonists, consistent with Bernard–Soulier syndrome, otherwise known as haemorrhagiparous thrombocytic dystrophy. Further testing revealed that

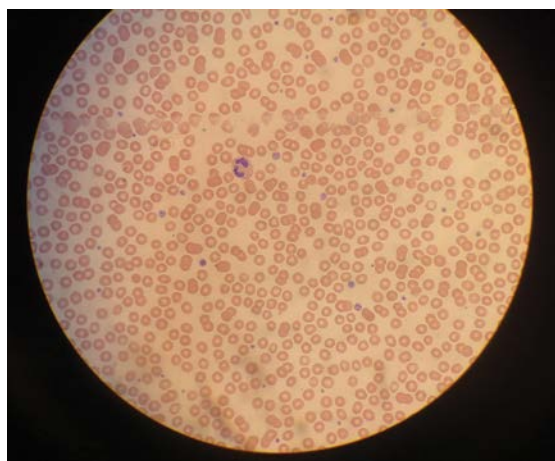
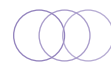


Figure 21.1 Blood film showing thrombocytopenia.

she had normal glycoprotein levels and a homozygous GP9 gene mutation. She was diagnosed with Bernard–Soulier syndrome variant.

Final diagnosis: Bernard–Soulier syndrome variant.

OUTCOME

The patient has since had multiple further admissions with migraines, which were felt to be triggering her vomiting and subsequent haematemesis. She is currently trialling treatment with tryptamine-based medication.

CASE DISCUSSION

Bernard–Soulier syndrome is an autosomal recessive condition characterised by thrombocytopenia, giant platelets and a prolonged bleeding time. The condition occurs due to defects of the platelet glycoprotein complex GPIb/V/IX, which is the receptor for von Willebrand factor. Platelet studies show reduced aggregation with ristocetin, even with the addition of normal plasma, unlike von Willebrand disease.

Although there is no specific treatment for Bernard–Soulier syndrome, tranexamic acid (an antifibrinolytic) can reduce the severity of bleeding episodes. Platelet transfusions can lead to the development of antiplatelet antibodies due to the presence of glycoprotein Ib/V/IX on the transfused platelets.

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CASE 22: A BLISTERING RASH

PATIENT HISTORY

A 22-year-old man presented to the emergency department with right leg swelling. He had returned 4 days earlier from a 3-week walking holiday in Ireland. Over the course of several days, his right ankle had become progressively more swollen and was now developing a blistering rash. The patient complained of severe pain and was now unable to weight bear. He was concerned that the swelling was extending to his right knee. While waiting in the emergency department, he noticed a rash developing over his arms and left leg. He had not taken any new medications, used any topical treatments on his leg or changed his bath products or washing detergent. The patient thought he had sustained an insect bite during his holiday to Ireland. His past medical history included depression, for which he took 50 mg sertraline OD. He was a non-smoker, denied any recreational drug use and usually drank minimal alcohol, but while in Ireland had consumed 20 units daily.

EXAMINATION

Initial observations: T 37°C, HR 107 bpm, BP 108/70 mm Hg, RR 14, SpO₂ 98% on room air.

The patient was alert and orientated and appeared generally well. His chest was clear to auscultation. His heart sounds were difficult to hear clearly due to tachycardia, but no murmurs were heard. His abdomen was soft and non-tender. He was neurologically intact. Examination of the right ankle identified a well-demarcated region of erythema, oedema and induration around the right ankle extending to the calf with multiple large, tense blisters (see [Figure 22.1](#)). There was an excoriated, maculopapular rash over the flexor surfaces of the arms and left leg.

INITIAL RESULTS

Routine blood tests: WCC 13.9, N^o 10.8, L^o 2.3, E^o 0.2, Hb 159, Plt 224, Na 135, K 4.1, Creat 77, CRP 11.

DIFFERENTIAL DIAGNOSES

The patient may have sustained an insect bite prior to developing the rash. If so, this is the likely source of infection, either via an immune response to the insect bite or by allowing pathogens to enter via the break in the skin. It sounds as though he has developed cellulitis of the right ankle. Causative agents are likely to include *Staphylococcus aureus* and *Streptococcus pyogenes*.

Erysipelas is another possibility. This is a bacterial infection of the dermis and hypodermis that extends to involve the cutaneous lymphatics. Patients classically have a very clearly demarcated area of erythematous skin with a significant amount of subcutaneous oedema present. The skin lesions appear more prominently raised and have clearer margins of involvement compared with cellulitis.

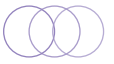


Figure 22.1 Multiple large, tense blisters on the patient's leg.

Blistering rashes can also include the autoimmune conditions, pemphigus and pemphigoid. Pemphigus develops due to the production of antibodies to desmoglein. The desmosomes cause epidermal cells to lose their adherent properties, leading to the formation of fragile bullae that slough off leaving painful eroded areas. Pemphigoid occurs due to the presence of IgG autoantibodies and presents with tense bullae.

Contact dermatitis can present with vesicular or bullous lesions. You should ask the patient if he has been exposed to any irritants, such as stinging nettles, during his walking holiday.

Necrotising fasciitis is a severe infection of the fascia that leads to necrosis of the subcutaneous tissues. The condition progresses rapidly and patients often develop signs of sepsis. The affected tissue appears erythematous, oedematous and is exquisitely tender, often described as causing pain that is disproportionate to the appearance of the skin lesion. Although the patient sounds systemically well, he does have an underlying tachycardia and his right ankle is very painful. Even if necrotising fasciitis is unlikely, it is important to consider and exclude this condition.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The first thing to do with any severe skin lesion is to exclude necrotising fasciitis. Careful examination of the lesion may reassure you, but if there is any doubt as to a possible diagnosis of necrotising fasciitis consider requesting a plastic surgery review. The skin should be swabbed for bacteria and ideally fluid from the blisters should also be obtained. This can be done by gently incising one of the lesions and collecting the fluid on a swab. Blood cultures must be taken, particularly if the patient develops a fever. Using a waterproof marker, draw around the outer margins of erythema to allow you to quickly identify extension or regression of the lesion.

An HIV test and a blood glucose level should be taken to identify any potential underlying immunosuppression. If the blood glucose level is elevated, a HbA1c level will need to be checked.



The patient is tachycardic and slightly hypotensive. Intravenous fluid resuscitation and broad-spectrum antibiotics should be commenced. Osteomyelitis may present with an overlying cellulitis so an x-ray of the ankle joint should be arranged.

CASE PROGRESSION

The surgical team reviewed the patient overnight and felt that necrotising fasciitis was unlikely. The patient was admitted under the medical team for further management. Intravenous antibiotics (co-amoxiclav) was commenced to treat a presumed cellulitis.

The swelling and oedema of the leg had increased by the following morning. The area of erythema had not extended. A Doppler ultrasound scan was performed; this excluded the presence of a deep vein thrombosis. X-rays of the right ankle and tibia/fibula showed no bony abnormalities.

The dermatology team reviewed the patient and aspirated fluid from several bullae. They subsequently diagnosed a bullous cellulitis of the right leg, likely secondary to an insect bite. They described a secondary id (autoeczematisation) reaction affecting the arms bilaterally and left leg.

Final diagnosis: Bullous cellulitis with secondary id reaction.

OUTCOME

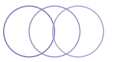
The patient required 5 days of intravenous antibiotics and the cellulitis gradually improved and all of the blistering lesions resolved. He was subsequently prescribed a 9-day course of oral antibiotics. His eczematous lesions were treated with emollients and topical steroids. He was followed up in the dermatology clinic as an outpatient 4 weeks later and had made a full recovery.

CASE DISCUSSION

Cellulitis usually develops following a breach to the skin's integrity or where there is an underlying element of immunosuppression. *Staphylococcus aureus* is the infectious agent that is most frequently isolated, but non-group A streptococcal infections are also common.

Isolating the causative agent via swabs and blood cultures is essential to providing targeted antibiotic treatment. Broad-spectrum penicillins are generally used as first-line agents until culture results become available.

Patients will usually present with an area of erythema that is hot to touch and has a degree of oedema. It is unusual to develop blistering lesions – this may signify a more severe infection that will put the patient at risk of sepsis. In these cases, methicillin-resistant *Staphylococcus aureus* (MRSA) or *Streptococcus pneumonia* infections should be in your list of potential diagnoses.



An id reaction is an eczematous, autoimmune response to an underlying infection, which is typically fungal in nature, but can be bacterial. Treatment should target the underlying infection (i.e. antifungal/antibiotic therapy), followed by topical or oral steroids for the rash related to the id reaction.

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CASE 23: HEART AND LUNGS

PATIENT HISTORY

A 66-year-old woman presented to the emergency department complaining of intermittent palpitations. The palpitations had been present for the past 3 months, initially occurring for a few seconds every couple of days but now lasting for several minutes 2–3 times daily. She also reported a 3-month history of dull, constant, right-sided chest pain. She had felt progressively more breathless and complained of unintentional weight loss over recent weeks. She denied any vomiting but was experiencing occasional diarrhoea. Her past medical history included peptic ulcer disease and osteoarthritis. She took regular 30 mg lansoprazole OD, 1 g paracetamol QDS and 30 mg dihydrocodeine QDS. She worked as an office manager, had a 40 pack year smoking history and drank 15–20 units of alcohol per week. She had travelled to France and Spain in the preceding 2 years.

EXAMINATION

Initial observations: T 36.5°C, HR 76 bpm, BP 110/70 mm Hg, RR 14 and SpO₂ 97% on room air.

The patient was alert and orientated. She appeared slim with an estimated body mass index of 19. Her chest was clear to auscultation. Her pulse rate was approximately 70 bpm and felt regular. Her heart sounds were normal and her jugular venous pressure (JVP) was not elevated. Her abdomen was soft and non-tender. A breast examination identified no lumps. A digital rectal examination found no abnormalities.

INITIAL RESULTS

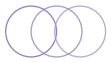
Routine blood tests: WCC 9.5, N° 7.1, L° 2.1, Hb 98, MCV 83, Plt 592, Na 134, K 4.7, Creat 45, Bili 7, ALT 20, ALP 272, CRP 92.

DIFFERENTIAL DIAGNOSES

The patient describes a history of intermittent palpitations with increasing frequency as well as unintentional loss of weight and occasional diarrhoea.

Hyperthyroidism should be at the top of the list of differential diagnoses. Hyperthyroidism can cause tachycardia and patients may subsequently develop arrhythmias such as atrial fibrillation and ventricular tachycardia. Other symptoms of hyperthyroidism may include diarrhoea, weight loss, tremor and thyroid eye disease.

A chronic infection could be driving the tachycardia and weight loss. The patient describes longstanding chest pain and dyspnoea. A chronic respiratory infection or empyema could be responsible for her symptoms. Tuberculosis should also be considered as a potential cause of shortness of breath, weight loss and general malaise. The patient has elevated inflammatory markers possibly in keeping with an infection, although the lack of cough would make this less likely.



Unintentional weight loss should always prompt consideration of a malignancy. In this case, the patient has a heavy smoking history in addition to describing shortness of breath, chest pain and diarrhoea. A primary lung malignancy or bowel cancer with lung metastases are possibilities.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient's thyrotropin (TSH) level should be measured to identify hyperthyroidism. An electrocardiogram (ECG) will show whether the patient is in sinus rhythm, atrial fibrillation, or another arrhythmia at present. Continuous cardiac monitoring will be more beneficial in identifying an abnormal rhythm that only occurs intermittently.

A chest x-ray should be performed to look for evidence of infection including tuberculosis, or a lung mass. If pneumonia is seen then antibiotic therapy can be commenced. If there is no obvious infection then a computed tomography (CT) scan of the chest may be considered to look for malignancy, possibly in addition to a scan of the abdomen and pelvis to identify sites of metastatic spread. If a lung mass is visualised on CT imaging then a sample of abnormal tissue or cells may be obtainable via bronchoscopy or CT-guided biopsy for histological analysis.

CASE PROGRESSION

The patient was admitted for further care under the medical team. An ECG showed sinus rhythm. A cardiac monitor was connected to identify any periods of arrhythmia. A septic screen was performed. A chest x-ray showed left upper zone airspace opacification and an area of increased density overlying the head of the left posterior fifth rib (see [Figure 23.1](#)). She remained well overnight but developed atrial fibrillation lasting for approximately 5 minutes running at 170 bpm in the morning.

A CT scan of her chest, abdomen and pelvis was performed to investigate for a possible primary lung malignancy and potential metastatic spread. The CT scan showed a large, spiculated mass in the left upper lobe consistent with a primary lung cancer. Pulmonary, adrenal, renal, liver and bone metastases were identified. A large pericardial effusion with a maximal depth of 18 mm was also identified (see [Figure 23.2](#)).

The patient became more short of breath and developed frequent runs of atrial fibrillation with a rapid ventricular response rate. She was treated with regular bisoprolol and remained in sinus rhythm following this.

A bronchoscopy showed a cobblestone appearance of the carina. The left main bronchus was significantly occluded by tumour. Bronchoscopy samples showed an adenocarcinoma infiltrating the mucosa.

The cardiology team inserted a pericardial drain and obtained blood-stained fluid. Cytology from the pericardial effusion showed malignant cells present, and the molecular testing confirmed adenocarcinoma. The patient felt much improved and was discharged home for outpatient follow-up. She returned to hospital 2 days later with severe shortness of breath and tachycardia. An echocardiogram showed a 3.4 cm effusion around right ventricle with signs of haemodynamic compromise (tamponade). Pericardiocentesis was repeated with

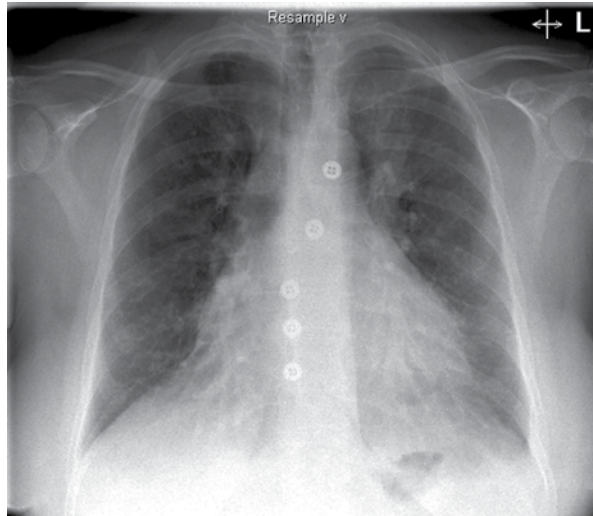


Figure 23.1 Chest x-ray showing left upper zone airspace opacification and an area of increased density overlying the head of the left posterior fifth rib.

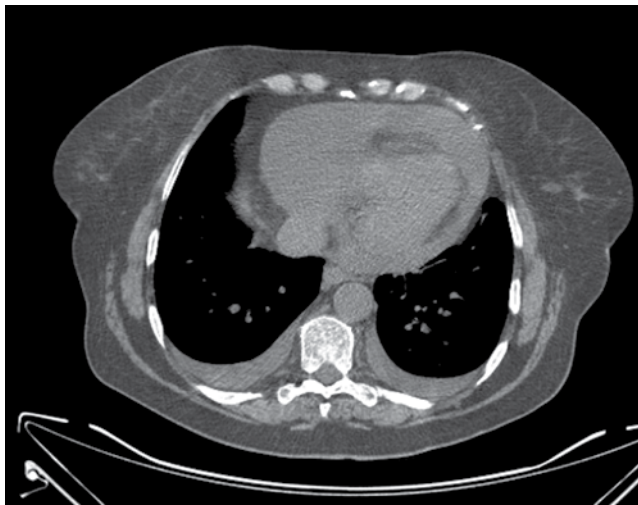
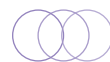


Figure 23.2 A CT chest image showing a pericardial effusion.

some symptomatic improvement, but the patient remained dyspnoeic on minimal exertion. A CT pulmonary angiogram confirmed the presence of multiple bilateral large pulmonary emboli.

Final diagnosis: Adenocarcinoma of the lung with widespread metastases and a malignant pericardial effusion.



OUTCOME

Following the patient's wishes, end-of-life care was commenced and she passed away 3 days later.

CASE DISCUSSION

Lung cancer is now the most commonly diagnosed cancer in the world. Adenocarcinoma accounts for around 40% of lung cancers. Patients typically present with symptoms that have come on insidiously many weeks or months earlier. Symptoms include cough, weight loss and dyspnoea.

Lung adenocarcinoma commonly metastasises to the bones, liver and adrenals. Malignant pericardial effusions are less common but are probably underdiagnosed. A large series of post-mortem examinations on over 1000 patients with known malignancy found that around 3% had a significant pericardial effusion. Adenocarcinoma was the most frequent cell type among the metastatic cardiac deposits.

As pericardial effusions increase, they can reach a critical stage, leading to haemodynamic compromise. In these cases, a pericardiocentesis may need to be carried out under echocardiographic guidance. If the patient develops recurrent, symptomatic pericardial effusions, the cardiothoracic surgeons may consider creating a pericardial window to allow fluid to drain into the pleural cavity.

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CASE 24: RECURRENT HAEMOTHORAX

PATIENT HISTORY

A 27-year-old woman presented to the emergency department complaining of shortness of breath. She described gradual-onset dyspnoea developing over the preceding 24 hours. She also complained of a 10-day history of a non-productive cough, fever and general malaise. Her past medical history included recent investigations for infertility. She was undergoing in vitro fertilisation (IVF) therapy and stated that a recent pelvic laparoscopy showed large fibroids and possible endometriosis. Her last menstrual period was 28 days ago. She took no regular medications and had no significant family history. She lived with her husband and worked as a jewellery designer. She had never smoked and did not drink alcohol. She had not travelled abroad in recent years.

EXAMINATION

Initial observations: T 36.5°C, HR 87 bpm, BP 108/71 mm Hg, RR 18 and SpO₂ 97% on FiO₂ 0.2.

The patient was alert and orientated. She appeared comfortable at rest and was talking in full sentences, but she became dyspnoeic on minimal exertion. Breath sounds were absent at the right base, which was noted to be dull to percussion. Heart sounds were normal and her jugular venous pressure (JVP) was not elevated. Her abdomen was soft and non-tender.

INITIAL RESULTS

Routine blood tests: WCC 4.4, N^o 2.3, L^o 1.5, Hb 144, Plt 265, Na 140, K 3.9, Creat 70, Bili 29, ALT 12, ALP 67, Alb 53, INR 1.0, CRP 2.

DIFFERENTIAL DIAGNOSES

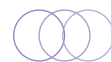
On examination, the patient has signs of a pleural effusion. She was well until 10 days earlier, when she developed fever and cough. A pneumonia with a parapneumonic effusion is a possible diagnosis, although her inflammatory markers are not elevated.

Lung cancer is a common cause of unilateral effusions but is unlikely in this case of a young woman who has never smoked. Breast cancer with a malignant pleural effusion is a possibility and she should have a breast examination to identify any obvious masses.

A pulmonary embolus with a pleural effusion developing due to local inflammation is also possible. IVF therapy may increase the risk of thromboembolism during the first trimester of pregnancy.

HOW WOULD YOU MANAGE THE PATIENT ACUTELY?

The patient should first have a β -HCG test, either using urine or blood, to determine whether she is pregnant. A chest x-ray should be requested, looking at the size of the effusion and whether there are other abnormalities such as consolidation or masses present. An



ultrasound-guided aspiration of pleural fluid should be performed and a chest drain sited if there is a large volume of fluid.

CASE PROGRESSION

The pregnancy test was negative. A chest x-ray showed a large right-sided pleural effusion with mediastinal shift. The respiratory team performed an ultrasound-guided pleurocentesis and aspirated black, viscous fluid. A drain was inserted and 750 mL dark fluid with clots was drained within 24 hours. A repeat chest x-ray showed significant resolution of the effusion. A computed tomography (CT) scan of the chest was performed, showing a moderate right-sided effusion and passive atelectasis of the right lower lobe.

A bronchoscopy was performed, but no abnormalities were identified and the cytology from bronchial washings showed normal cells. The patient had improved symptomatically and was therefore discharged home. She re-presented 4 weeks later with a recurrence of the right-sided pleural effusion. Again, viscous bloody fluid was aspirated from her pleural space. A video-assisted thoracic surgical pleurodesis was performed. Samples of pleural biopsies showed endometrial tissue.

Final diagnosis: Pleural endometriosis with catamenial haemothorax.

OUTCOME

An outpatient magnetic resonance imaging (MRI) pelvis scan to coincide with menstruation confirmed pelvic endometriosis. Since pleurodesis was performed, the patient has not had further episodes of haemothorax.

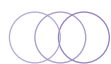
CASE DISCUSSION

Thoracic endometriosis can present in a variety of ways, including catamenial pneumothorax and catamenial haemoptysis. Her recent fertility treatment may have triggered the presentation by altering the patient's baseline sex hormone levels.

Catamenial haemothorax classically presents within 72 hours of menstruation onset. The diagnosis is rarely made on CT, but MRI shows lesions with homogenous high signal in T1- and T2-weighted images. Hormonal treatment (to suppress ovulation) is the mainstay of treatment. Video-assisted thoracoscopic surgery will allow endometrial blebs, usually on the parietal pleura, to be treated with diathermy. Alternatively, if diaphragmatic defects are permitting abdominal endometrial blood to enter the pleural space, mesh can be applied over the base of the diaphragm to reduce the transit of blood.

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CASE 25: FEVER AND UNILATERAL WEAKNESS

PATIENT HISTORY

A 70-year-old woman was brought into hospital by the ambulance service after being found vomiting and responding to auditory hallucinations in the street. The patient was agitated and distressed and declined to give further history regarding her presentation to hospital. She told the team that she had been travelling around Europe as a missionary for the past 25 years, had arrived in the United Kingdom from Greece 2 weeks ago, and had since been living in bus shelters. No further history could be elicited. A passport was found in her bag with recent Greek and Italian stamps. She refused to participate with mental state or capacity assessments.

EXAMINATION

Initial observations: T 39°C, HR 82 bpm, BP 118/39 mm Hg, RR 18 and SpO₂ 96% on room air.

The patient was visibly distressed and agitated. She appeared cachectic with an estimated body mass index (BMI) of 17. On examination of her chest, bi-basal crackles were heard. An ejection systolic murmur was heard around the aortic region that did not radiate to the carotid arteries. There was no peripheral oedema. The patient did not tolerate examination of the jugular venous pressure (JVP), but it did not appear elevated. The patient was moving all four limbs and had good power throughout. Plantars were down going bilaterally. Her pupils were equal and reactive to light and there was no facial asymmetry. She was not photophobic and had no neck stiffness. No further neurological examination was possible at this time.

INITIAL RESULTS

Routine blood tests: WCC 6.0, Hb 80, MCV 73, Plt 253, Na 134, K 4.9, Creat 71, CRP 27.

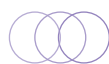
Urine dipstick test: no abnormalities.

Computed tomography (CT) head scan: small vessel disease, no acute intracranial event.

DIFFERENTIAL DIAGNOSES

The patient presents with a high fever and confusion. She has a normal white cell count but an elevated C-reactive protein (CRP). The confusion may represent longstanding dementia or cognitive impairment, but without further information we must assume that the patient has delirium, possibly precipitated by an infection. She has a heart murmur, which may be new – bacterial endocarditis is therefore a possible diagnosis. The initial examination has not identified whether peripheral stigmata of endocarditis, such as Osler's nodes or splinter haemorrhages, are present. Another possibility is that the patient is febrile and confused due to an encephalitic process.

Thyrotoxicosis is another leading differential diagnosis. This condition can cause fever, confusion and weight loss – potentially explaining why the patient appears cachectic.



The patient may be withdrawing from alcohol. She is agitated and unable to give us any further history regarding her social situation, including alcohol intake. Her fever is rather high for a pyrexia simply related to alcohol withdrawal, however.

Neuroleptic malignant syndrome can occur in patients on potent neuroleptics, such as haloperidol, particularly if the dosage has recently increased, or those withdrawing from anti-Parkinson's medications (due to an abrupt reduction in dopaminergic activity). Patients present with fever, rigidity and confusion or agitation and will eventually progress to autonomic dysfunction due to excessive dopamine blockade.

Serotonin syndrome can develop in patients who have overdosed on serotonergic agents or those on combinations of drugs that increase serotonin levels. Serotonergic drugs include monoamine oxidase inhibitors, tricyclic antidepressants and selective serotonin re-uptake inhibitors. Patients develop high fevers, agitation, clonus, myoclonus, tremor and hyperreflexia.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

Assume the patient has an acute delirium and try to nurse her in a well-lit, quiet room, minimising the number of staff members that attend the patient. If possible, a collateral history should be obtained to establish her normal cognitive status, whether she has any underlying medical conditions and what medications she may be taking.

A septic screen including blood cultures and a chest x-ray will need to be performed. Her creatine kinase (CK) level should be checked as this can be elevated in neuroleptic malignant syndrome. Her thyroid function, vitamin B₁₂, folic acid and calcium levels should also be checked as potential causes of confusion. Syphilis and HIV serology should be sent to the virology laboratory.

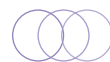
If there is no clear focus of infection, a lumbar puncture will need to be attempted if the patient will tolerate the procedure. Treatment for presumed encephalitis should be commenced with intravenous aciclovir. An echocardiogram can be requested to investigate her heart murmur, looking for vegetations indicative of endocarditis.

CASE PROGRESSION

A chest x-ray was unremarkable. Thyroid function and calcium levels were within the normal range. The patient was intermittently confused over the next 12 hours. She was diagnosed with an acute delirium secondary to an unknown infection based on her fluctuating cognition and agitation. She was treated with aciclovir to cover for possible encephalitis and broad-spectrum antibiotics to treat a presumed bacterial infection.

After 24 hours of admission she was less confused and demonstrated capacity to refuse a lumbar puncture and further antibiotic and antiviral therapy. She informed the team that she had been sleeping on the streets and was keen to return to some friends that she had been with. She requested discharge and declined advice about local homelessness support.

Immediately prior to her discharge, the patient developed new right arm weakness. Following a repeat assessment, two consultants documented that she now lacked capacity regarding her health care. She was sedated and a repeat CT scan of her head showed new left middle cerebral artery infarction. Later that afternoon, she became drowsy and incoherent, developing a left-sided facial droop and left arm and leg weakness.



A transthoracic echocardiogram identified large vegetations over her mitral and aortic valves. Intravenous benzylpenicillin, gentamicin and vancomycin were commenced. Blood cultures taken at admission eventually grew *Bartonella henselae* and her antibiotic treatment was modified accordingly.

Final diagnosis: *Bartonella* endocarditis leading to septic emboli and subsequent cerebral infarction.

OUTCOME

The patient was transferred to a specialist stroke ward where she received intensive neurophysiotherapy. She made a surprisingly good recovery and was able to walk safely and talk with normal speech after 8 weeks of inpatient therapy.

Further history taking established that the patient had cared for a large number of stray cats while in Greece and had sustained repeated injuries from cat scratches and bites. She refused to consider surgical options for treatment of her endocarditis and self-discharged against medical advice when she felt that she could independently manage activities of daily living.

CASE DISCUSSION

Bartonella henselae, also known as cat scratch fever, has a worldwide distribution, with the domestic cat acting as a major reservoir. Cat bites may transmit *Bartonella henselae* via infected cat saliva and cat scratches can transmit the infection via flea faeces containing *Bartonella henselae*. Ticks may also act as reservoirs for the infection. The infection typically presents with lymphadenopathy, fever and malaise, but encephalopathy and endocarditis are also relatively common manifestations.

Bartonella infections are particularly common among homeless people and those with poor living conditions where ticks and cats with fleas are present. People with underlying immunosuppression are more likely to contract the infection.

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CASE 26: A CASE OF PAROTITIS FOLLOWED BY ACUTE HEARING LOSS

PATIENT HISTORY

A 57-year-old man presented to the emergency department complaining of a worsening cough. The cough had been present for approximately 2 weeks and was productive of green sputum. He had seen his general practitioner 1 week earlier and taken a course of amoxicillin for a presumed lower respiratory tract infection with no improvement of symptoms. He was febrile throughout the day and reported experiencing frequent headaches and a feeling of general malaise. He had been unable to eat solid food for the last 48 hours due to facial pain on chewing. He denied any past medical history and took no regular medications. He worked as a cashier in a supermarket and had never smoked. He had not travelled abroad for more than a decade.

EXAMINATION

Initial observations: T 38.4°C, HR 88 bpm, BP 130/85 mm Hg, RR 18, SpO₂ 96% on room air.

The patient was alert and orientated but appeared flushed. His chest was clear to auscultation. His heart sounds were normal and there were no signs of peripheral oedema. His abdomen was soft and non-tender. There was bilateral, palpable cervical lymphadenopathy with the largest node measuring approximately 2 cm in diameter in the left submandibular region. His pharynx appeared erythematous. There was no tonsillar swelling or exudate. The parotid glands were swollen bilaterally and the overlying skin appeared erythematous.

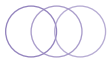
INITIAL RESULTS

Routine blood tests: WCC 17.6, N^o 15.4, L^o 1.1, Hb 125, Plt 296, Na 135, K 3.8, Creat 69, CRP 17.

DIFFERENTIAL DIAGNOSES

The patient describes symptoms of fever, malaise, cough and pain around his face and neck. Examination has identified parotitis. It would be useful to know from the history whether the patient has had similar episodes in the past as the differential diagnosis for an isolated event of acute parotitis is different from that of recurrent or chronic parotitis.

Assuming this is his first episode of parotitis, the patient may have developed a bacterial or viral infection. Acute suppurative parotitis is most commonly caused by *Staphylococcus aureus* and can lead to severe sepsis if left untreated. Appropriate antibiotics should be prescribed, in addition to intravenous fluid rehydration, and urgent drainage should be performed. Viral parotitis is most commonly caused by the mumps virus, although this condition is now uncommon due to widespread vaccination programmes. Viral parotitis can also be caused by influenza and enteroviruses.



Chronic recurrent parotitis is typically caused by similar organisms to the acute form but can also be mistaken for Sjögren's syndrome. Rarely, both tuberculosis and HIV infection can cause a chronic parotitis that develops insidiously and tends to be painless. In patients with HIV, parotitis arises due to the development of lymphoepithelial lesions.

Autoimmune conditions such as Sjögren's syndrome can cause a chronic parotitis. The parotid gland may be tender in Sjögren's syndrome and is related to lymphocytic infiltrates within the salivary glands. Bilateral parotitis can also be one of the presenting features of sarcoidosis, prior to the development of more classical symptoms and signs.

Obstruction of the parotid with a salivary stone can occur but this tends to present with unilateral swelling. Neoplastic disease is also usually unilateral.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient has a high fever and elevated inflammatory markers. A basic septic screen (blood cultures, chest x-ray and urine culture) should be organised. Broad-spectrum antibiotics should be commenced, to cover for a possible primary *Staphylococcus aureus* parotitis or parotitis due to other organisms such as anaerobes or *Enterobacter*. He should be isolated in case this is mumps and a vaccine history should be taken. Salivary swabs for mumps should be collected.

He describes difficulty swallowing and should thus receive intravenous fluids if his oral intake is limited. Paracetamol will treat the pain and reduce his fever. Heat packs may provide symptomatic relief and improve drainage of pus from the glands. An ear, nose and throat (ENT) specialist review should be requested to assess the parotitis and consider commencing sialogogues (agents that increase salivary flow) or surgical intervention.

CASE PROGRESSION

The patient reported a penicillin allergy and was therefore commenced on clarithromycin antimicrobial therapy. A chest x-ray showed no focal consolidation and blood cultures showed no growth at 48 hours. He continued to have high fevers reaching 39.8°C on the second day of admission. Gentamicin was commenced to provide antibiotic cover against potential gram-negative organisms. The ENT team advised continuing antibiotics and other supportive measures.

On the third day of admission, the patient developed left-sided epididymo-orchitis. The virology team reviewed the patient and arranged for mumps virus swabs and serological testing to be performed. The following day, the patient was continually spiking fevers of 40°C with minimal relief from paracetamol and intravenous fluids. He complained of pain around his right ear and shortness of breath. On examination, there were reduced breath sounds at the base of the left lung and his right ear appeared erythematous and swollen externally. Otoscopy was unremarkable. A chest x-ray showed left basal consolidation.

Over the next 48 hours, the patient developed left-sided hearing loss and continued to have right-sided ear pain. Supportive therapy for presumed mumps infection was continued. The ENT team re-reviewed the patient and identified left-sided sensorineural hearing loss, which was subsequently confirmed on formal audiometry (see [Figure 26.1](#)). Corticosteroid therapy was commenced. The ENT team arranged a magnetic resonance imaging (MRI) scan, which

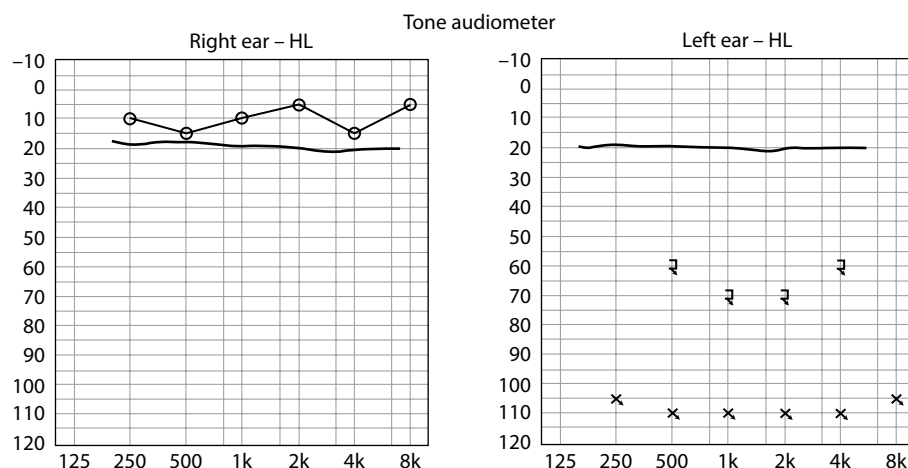


Figure 26.1 Audiometry study.

showed subtle changes to the fluid in left membranous labyrinth, suggestive of an exudate. Mumps virus serology returned confirming an acute infection.

Final diagnosis: Mumps infection.

OUTCOME

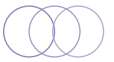
The patient's symptoms of fever and parotitis gradually resolved. A repeat chest x-ray 4 weeks later showed complete resolution of his left basal pneumonia. His left-sided hearing loss did not improve.

CASE DISCUSSION

The mumps virus is part of the Paramyxoviridae virus family. Outbreaks are becoming increasingly frequent, particularly among university students. In the late 1990s, data which incorrectly associated the measles, mumps and rubella (MMR) triple vaccination with the development of autism led to a significant reduction in vaccination uptake in the United Kingdom and a resurgence of mumps disease. Vaccination uptake has since returned to near-normal levels, with more than 90% of eligible children receiving the MMR immunisation.

Mumps virus infection results in epididymo-orchitis in 30% of cases in males, and around half of these experience testicular atrophy, although long-term fertility problems are uncommon. Female patients may develop oophoritis and there is a 27% risk of spontaneous abortion in women infected during their first trimester of pregnancy. Rarely, mumps meningitis or encephalitis may develop.

Mumps virus infection is among the most common causes of unilateral acquired sensorineural hearing loss in children and young adults. If symptoms of otitis or impaired hearing develop, steroid therapy should be commenced immediately as this can dramatically improve the outcome of sensorineural hearing loss.



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CASE 27: A PURPURIC RASH

PATIENT HISTORY

A 67-year-old man presented to hospital with a rash covering his legs. He said the rash had developed over the course of several days and was spreading from his feet up toward his trunk. The rash was not pruritic or tender to touch. He denied any fevers, cough or shortness of breath. He had not been exposed to any chemicals or changed his usual toiletry products or detergents. For 1 week preceding the rash, the patient had been experiencing pain around the small joints of his hands and swelling of both knees bilaterally. His past medical history included a 2-year history of intermittent episodes of abdominal discomfort that had been investigated extensively at his local hospital and diagnosed as irritable bowel syndrome. He took mebeverine for his occasional abdominal pain but no other medications. He was a retired social worker who neither drank alcohol nor smoked tobacco. He had travelled to Egypt 18 months earlier but had not been abroad since.

EXAMINATION

Initial observations: T 37.2°C, HR 72 bpm, BP 134/90 mm Hg, RR 16 and SpO₂ 98% on room air.

The patient was alert and orientated. He was afebrile. His chest was clear to auscultation and his heart sounds were normal. His abdomen was soft but generally tender on palpation, particularly around the umbilical region. Neurological examination was unremarkable. The small joints of the hands and the knees were tender but not particularly swollen. There was a florid, violaceous rash covering the lower limbs. The rash consisted of 5–10 mm lesions that were well demarcated and non-blanching (see [Figures 27.1](#) and [27.2](#)).

INITIAL RESULTS

Routine blood tests: WCC 8.9, Hb 146, Plt 89, Na 139, K 3.9, Creat 110 (no baseline results available), CRP 45.

DIFFERENTIAL DIAGNOSES

Idiopathic thrombocytopenic purpura presents with a purpuric rash with a history of bleeding (epistaxis, bleeding from gums when brushing teeth and menorrhagia) and easy bruising. A very low platelet count (e.g. less than $30 \times 10^9/L$) would be expected in this autoimmune condition. The patient has a purpuric, maculopapular rash. Palpable purpura may develop in vasculitis following erythrocyte extravasation. Vasculitis can be divided into four subtypes: large, medium, small and medium, and small vessel vasculitis.

Large vessel vasculitis includes giant cell arteritis (GCA) and Takayasu's arteritis. GCA presents with headache, scalp tenderness and jaw claudication and is often associated with shoulder and pelvic girdle pain, typical of polymyalgia rheumatic. Takayasu's arteritis is a vasculitis predominantly affecting the carotid and vertebral arteries and the aorta. Symptoms include

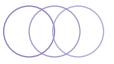


Figure 27.1 Violaceous rash covering the patient's lower limbs.

headache, fever and arthralgia. Typical examination findings are hypertension, carotid bruits and a significant difference in blood pressures between the left and right arms. Aside from palpable purpura, patients can develop areas of ulceration and necrosis.

Medium vessel disease includes polyarteritis nodosa (PAN) and Kawasaki's disease. Symptoms of PAN include weight loss, abdominal and testicular pain and mono- or polyneuropathies. Blood tests may show impaired renal function. There is a strong association between hepatitis B infection and PAN. Kawasaki's disease almost universally affects young children rather than teenagers and adults. It presents with fever and lymphadenopathy and children often have mucous membrane changes and desquamation of their fingers. Patients with medium vessel vasculitis may develop subcutaneous nodules and livedo reticularis in addition to purpura.

Small and medium vessel vasculitis (without immune complex deposition). The antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides come under this category, including granulomatosis with polyangiitis (GPA, formerly Wegener's granulomatosis), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA, formerly Churg-Strauss syndrome). GPA involves the upper and lower respiratory tract and the kidneys. Patients can present with rapidly progressive glomerulonephritis, subglottal stenosis, epistaxis and pulmonary haemorrhage. Diagnosis is aided by the presence of cytoplasmic anti-neutrophil cytoplasmic antibody (c-ANCA) directed against proteinase 3 (PR3) and granulomas on renal or lung biopsy. Patients with MPA have the usual constitutional symptoms associated with vasculitis but may also demonstrate a widespread myalgia and mononeuritis multiplex. p-ANCA is more commonly associated with MPA compared with c-ANCA. Patients with EGPA typically develop allergic rhinitis, asthma and eosinophilia. Mono- or polyneuropathy may be present.

Small vessel vasculitis includes Henoch-Schönlein purpura (HSP) and cryoglobulinaemia. HSP is an immunoglobulin A-mediated disorder that classically affects children,



Figure 27.2 The raised lesions were well-demarcated and varied from 5–10 mm in diameter.



presenting with a tetrad of abdominal pain, arthralgia, abdominal pain and renal impairment. Cryoglobulinaemia has a strong association with hepatitis C virus infection. Patients present with acrocyanosis, renal failure, Raynaud's phenomenon and arterial thrombosis. Diagnosis is made by the detection of cryoglobulins in the serum.

Other causes of vasculitis include drug reactions, malignancy and HIV infection.

It is clear that this patient has an underlying cutaneous vasculitis. His main symptoms and signs include longstanding abdominal pain, an acute arthralgia and mild, chronic renal impairment. HSP is the most likely unifying diagnosis.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient should be admitted for further investigations. Blood tests should be sent to test for routine autoantibodies (anti-nuclear antibodies [ANA], anti-extractable nuclear antigen [ENA], gastric parietal cell antibodies, mitochondrial antibodies, liver-kidney microsomal antibodies and smooth muscle antibodies) as well as immunoglobulins and cryoglobulins (remember to take and deliver the sample using a warmed tube that is kept at 37°C until the blood is processed). Blood should also be tested for the presence of ANCAs, rheumatoid factor, lupus anticoagulant, anti-cardiolipin and anti-β₂-glycoprotein-I.

He should be screened for infections, including HIV, hepatitis B and hepatitis C. X-rays of the painful joints may show underlying arthritic changes. If he remains stable over the next 24–48 hours, he may be discharged home to be followed up in a few days' time as an outpatient.

CASE PROGRESSION

The patient was reviewed by the rheumatology team who ordered the aforementioned blood tests, as well as a Paul Bunnell test, antistreptolysin O titre and blood cultures, and suggested that the clinical findings may be compatible with a diagnosis of HSP. The dermatology team reviewed the patient. They felt the rash could either represent idiopathic thrombocytopenic purpura (ITP) or HSP, with the former diagnosis being more likely. A skin biopsy was taken.

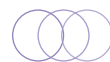
While in hospital, the patient had a further episode of abdominal discomfort. The pain settled with simple analgesia. An abdominal ultrasound was unremarkable. The patient felt better by the following morning and was discharged home.

He was followed up in the outpatient clinic 1 week later. His skin biopsy showed a leucocytoclastic vasculitis with perivascular IgA deposition, consistent with a diagnosis of HSP.

Final diagnosis: HSP.

OUTCOME

The patient was treated with corticosteroids, assuming that his renal impairment was secondary to underlying HSP. The rheumatology team thought that his intermittent episodes of abdominal pain that had developed over the preceding 2 years may be related to HSP rather



than irritable bowel syndrome. He was followed up for 6 months and has had no further recurrence of purpura. His renal impairment resolved.

CASE DISCUSSION

HSP is an IgA vasculitis that predominantly affects children and young adults. The acute phase of HSP is preceded by an upper respiratory tract infection in up to 50% of cases. Patients present with abdominal pain, palpable purpura, arthralgia and renal impairment. In severe cases, gastrointestinal haemorrhage, bowel ischaemia and bowel perforation may occur.

The American College of Rheumatology criteria for the diagnosis of HSP are two or more of the following: age at onset of greater than 20 years, palpable purpura, acute abdominal pain and histopathology showing granulocytes in the walls of small arterioles or venules.

Diagnosis is based on the clinical picture and, ideally, a skin or renal biopsy showing leucocytoclastic vasculitis with IgA deposition.

Conservative management, with simple analgesia and fluids forms the mainstay of treatment in simple cases of HSP. Patients with severe disease, such as those with renal failure or gastrointestinal haemorrhage, may benefit from corticosteroid therapy.

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CASE 28: BILATERAL HIP PAIN

PATIENT HISTORY

A 64-year-old woman presented to the emergency department complaining of lower back and bilateral hip pain. She explained that she had noticed that she had lower back pain around 6 months ago, following exertion or short periods of immobility. The lower back pain was now present for most of the day and was becoming increasingly severe. She also described bilateral hip pain that had been present for around 3–4 months. This was initially only present when she was walking upstairs or on a gradient but was now limiting her mobility indoors. She had been unable to attend her job as a seamstress for the past 2 months due to the worsening pain. She denied any preceding injuries. She had no symptoms of fever. On direct questioning, she described night sweats and 7 kg unintentional weight loss within the past 4–6 weeks. She denied altered sensation or episodes of incontinence. Her past medical history included pulmonary tuberculosis, which was treated 2 years earlier, and vitamin D deficiency. She took intermittent courses of cholecalciferol. She looked after her grandchildren on weekdays. She travelled to Bangladesh every summer and stayed with family in Dhaka for 4 weeks. She had last travelled there 9 months earlier. She denied smoking tobacco or drinking alcohol.

EXAMINATION

Initial observations: T 37°C, HR 68 bpm, BP 146/88 mm Hg, RR 16 and SpO₂ 96% on room air.

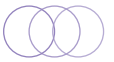
The patient was alert and orientated. She appeared comfortable at rest. Her chest was clear to auscultation. Her heart sounds were dual with no murmurs. Her abdomen was soft and non-tender. Neurological examination, including perianal sensation and anal tone were normal. Tenderness was noted on palpation around the iliac crests and sacroiliac joints bilaterally. Both hip joints had full range of movement, but there was pain on extremes of hip flexion, extension, internal rotation and external rotation bilaterally. There was point tenderness over L4/L5.

INITIAL RESULTS

Routine blood tests: WCC 3.0, N^o 1.6, L^o 1.1, Hb 86, MCV 104, Plt 112, Na 139, K 4.0, Creat 87, Bili 12, ALT 33, ALP 158, cCa 2.35, PO₄ 1.5, CRP 23.

DIFFERENTIAL DIAGNOSES

The patient presents with lower back and bilateral hip pain. Her condition has progressed over several months. The most common cause of hip pain in patients of this age is an arthritis. Osteoarthritis typically presents in or after the sixth decade of life and its prevalence increases with age. X-rays should be performed to confirm the diagnosis and assess the severity. X-ray features of osteoarthritis include loss of joint space, osteophyte formation, subchondral sclerosis and cyst formation. The patient should be thoroughly examined to



assess for signs of other arthritides, such as rheumatoid or psoriatic arthritis, and questioned regarding the presence of systemic features of these diseases.

Polymyalgia rheumatic (PMR) is another likely diagnosis. This condition is characterised by myalgia involving the shoulder and pelvic girdle with morning stiffness. The underlying inflammatory process commonly causes symptoms of fever and weight loss, both of which are features of this patient's presentation.

Haematogenous spread of tuberculosis can lead to infection within the vertebrae, causing a tuberculosis spondylitis, also known as Pott disease. The patient has had pulmonary tuberculosis 2 years earlier and she both lives in and travels to cities with a high prevalence of tuberculosis (London and Dhaka). This diagnosis could explain the night sweats and weight loss, as well as the pancytopenia if bone marrow involvement is present.

Malignancy with bony metastases is another possibility. Breast cancer is a common malignancy in female patients of this age group. Further examination may identify an abnormal mass or the presence of lymphadenopathy.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

A focussed clinical examination should be performed, assessing for the presence of cervical, axillary or inguinal lymphadenopathy, breast masses, rashes, and tenderness or swelling of her other joints. The patient is pancytopenic and a blood film should therefore be requested.

X-rays of the chest, thoracic and lumbar spine, pelvis and hip joints should be performed. The chest x-ray may show new changes associated with tuberculosis infection or evidence of a primary or secondary lung malignancy. X-rays of the lumbar spine, pelvis and hips may identify fractures, lytic lesions or evidence of arthritic changes.

Depending on the results of the above investigations, further imaging may be required, for example a staging computed tomography (CT) scan if malignancy is thought to be likely.

CASE PROGRESSION

A chest x-ray showed a right apical cavitating lesion that was unchanged compared with previous films. Pelvic and hip x-rays showed degenerative changes at both hip joints with narrowing of the joint space and marginal osteophytosis, consistent with osteoarthritis. A lateral spine x-ray revealed an anterior wedge fracture at the level of T4/T5 and loss of vertebral height at T12 through to L3. A myeloma screen was performed – the immunoglobulin levels were within normal range and there were no Bence Jones protein in the urine.

A diagnosis of osteoarthritis of the hips with a wedge fracture of T4/T5 was made. The patient responded well to simple analgesia and physiotherapy. Calcium and vitamin D supplementation was commenced and an outpatient bone density scan was booked to assess for the presence and severity of osteoporosis, as well as a magnetic resonance imaging (MRI) scan of the whole spine. The patient was discharged home.

The MRI scan of her spine performed 2 weeks later showed multilevel abnormalities with enhancing extradural soft tissue masses seen throughout the spinal column, involving T4–T6 and T8. Multiple fractures were seen in association with this. There was cord compression seen at the level of T4 and imminent cord compression at the T12 level. She was readmitted to



hospital for further investigation. At this stage, lymphoma, metastatic disease and tuberculosis were considered to be the most likely diagnoses.

Dexamethasone 8 mg twice daily was commenced and gradually tapered to 4 mg BD, which she continued on for several weeks. The local neurosurgical unit was contacted but felt that surgical intervention was not warranted at this stage as the patient had no neurological symptoms and no confirmed tissue diagnosis.

A CT scan of the patient's chest, abdomen and pelvis identified extensive lytic areas within the pelvis and vertebrae and extraosseous bony disease. There were old tuberculosis-related changes within both lung apices. A bone scan showed multiple foci of tracer uptake in the ribs bilaterally and increased uptake in the right humerus and proximal femora, highly suspicious of malignant bone involvement.

The haematology team performed a bone marrow aspiration, which showed less than 1% plasma cells, making a diagnosis of myeloma unlikely. A trephine sample was taken for further analysis.

A CT-guided iliac bone biopsy of a lytic lesion was performed via interventional radiology. The patient was discharged home for follow up with the oncology team within 1 week. The bone trephine results were available at this stage, showing 80% plasma cell infiltration and the CT-guided bone biopsy sample showed 15% plasma cell infiltration, consistent with a diagnosis of non-secretory myeloma.

Final diagnosis: Non-secretory myeloma.

OUTCOME

The patient was commenced on a 4–6 month regime of chemotherapy (bortezomib, thalidomide and dexamethasone) and is now being considered for an autologous stem cell transplant.

CASE DISCUSSION

Non-secretory myeloma is a rare variant of myeloma, affecting around 1% of patients with multiple myeloma. Patients have no detectable paraprotein or serum free light chain abnormalities, making the diagnosis challenging.

Patients with non-secretory myeloma have a similar or improved prognosis compared to those with secretory myeloma. Monitoring disease progress can be challenging, and computed tomography-positron emission tomography (CT-PET) scans are often used to assess disease response at regular intervals.

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CASE 29: BLEEDING GUMS

PATIENT HISTORY

A 45-year-old woman was referred to hospital by her general practitioner after presenting with bleeding gums, epistaxis and a feeling of general malaise. She described a week-long history of epistaxis occurring three to four times daily. Her gums had started to bleed for several minutes after brushing her teeth for the past few days. She described feeling very fatigued and nauseated. She had vomited earlier that morning and described a dull ache around her umbilical region. The general practitioner performed some routine blood tests and found that her urea level was very elevated at 57 mmol/L and her creatinine level was 189 μ mol/L. A baseline test from 6 years earlier showed a creatinine level of 56 μ mol/L. The doctor called the patient and advised her to present to the emergency department urgently for further assessment. Over the past few months, the patient had been reviewed with worsening right leg pain and fatigue. X-rays of her hip, femur and knee had been unremarkable. Her past medical history included two first-trimester miscarriages. She had been using 400 mg ibuprofen TDS for the past 6 weeks but took no other regular medications. Her family history was significant for both her mother and sister having systemic lupus erythematosus (SLE). She worked as a baker, was an ex-smoker with a 10 pack year history and did not drink alcohol. She lived with her husband and two young children. She had been born in the United Kingdom and had last travelled abroad to Belgium 8 months ago.

EXAMINATION

Initial observations: T 37°C, HR 95 bpm, BP 168/108 mm Hg, RR 20 and SpO₂ 100% on room air.

The patient appeared pale and lethargic. There was fresh blood on the gums and teeth but no clear bleeding points. There was old blood around the nostrils. Her chest was clear to auscultation. Her heart sounds were normal and there were no signs of peripheral oedema. Her abdomen was soft and non-tender, with normal bowel sounds. The right hip was tender on both flexion and extension but normal range of movement was preserved.

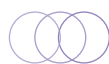
INITIAL RESULTS

Routine blood tests: WCC 7.0, N^o 5.2, L^o 1.5, Hb 89, Plt 383, Na 135, K 5.6, Creat 209, Bili 15, ALT 17, ALP 40, INR 1.2, APTT 1.1, CRP 20.

DIFFERENTIAL DIAGNOSES

The patient has presented with a severe kidney injury with uraemia. Her peripheral blood counts show normal platelet levels and her coagulation screen is also normal. The bleeding from her gums and nose could be due to platelet dysfunction induced by uraemia. See the case discussion for further information about uraemia-induced platelet dysfunction.

The patient has had right hip and leg pain for several months and has been taking 1.2 g ibuprofen daily for the past 6 weeks. Non-steroidal anti-inflammatory drugs (NSAIDs) can



cause an acute kidney injury via a variety of mechanisms. A hypersensitivity reaction to certain drugs, including NSAIDs, can lead to the development of nephritis and renal papillary necrosis. NSAIDs also cause significant inhibition of prostaglandin production (via cyclooxygenase inhibition), some of which are involved in the maintenance of renal blood flow leading to a reversible acute kidney injury.

The patient has a strong family history of SLE. She has had multiple spontaneous abortions. It may be that she has SLE, or possible anti-phospholipid syndrome (APLS). If this is the case, a lupus nephritis should be suspected.

The patient has elevated blood pressure at presentation (168/108 mm Hg). Her hypertension may be longstanding and could thus result in hypertensive nephropathy or nephrosclerosis. This occurs when chronic arterial hypertension leads to increased hyaline deposition along the walls of arteries and arterioles, reducing their luminal diameter and thus glomerular blood flow. Glomerular ischaemia follows, with subsequent impairment of renal function.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

This patient will need frequent monitoring of her renal function with close attention paid to her sodium and potassium levels and acid–base status (via a blood gas sample). She has an elevated serum potassium level. If this continues to rise or the patient develops an acidosis, renal replacement therapy (RRT) may need to be considered. Her fluid balance should be documented via an input and output chart. A urinary catheter should ideally be inserted to allow hourly recording of her urine output.

Intravenous fluids should be commenced. Assuming her blood gas sample shows a normal pH, bicarbonate level and base excess, normal saline would be the fluid of choice. Be aware that the patient may easily become fluid overloaded. A fluid challenge (e.g. 500 mL normal saline over 30 minutes) should be given initially and her fluid status can then be reassessed prior to continuing further fluid therapy. An urgent renal ultrasound scan must be requested to look for an obstructive cause of her renal impairment or any other obvious pathology.

Blood tests will need to be sent to investigate for potential underlying causes of renal impairment, including anti-nuclear antibodies (ANA), anti-neutrophil cytoplasmic antibody (ANCA), anti-glomerular basement membrane (GBM), immunoglobulins, serum protein electrophoresis, C3 and C4, creatine kinase (CK), erythrocyte sedimentation rate (ESR), anti-cardiolipin antibodies and lupus anticoagulant, HIV and hepatitis tests. Urine should be sent for light chains and casts.

If her blood pressure remains elevated, an antihypertensive agent, ideally a calcium channel blocker, should be commenced.

CASE PROGRESSION

A renal ultrasound scan showed bilaterally oedematous kidneys with loss of corticomedullary differentiation and a hypoechoic lesion in the right mid-pole (see [Figure 29.1](#)). The patient's urea and creatinine levels continued to climb over the following 48 hours. She maintained

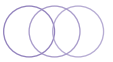


Figure 29.1 Renal ultrasound scan showing hyperechoic lesion.

a good urinary output of 60 mL/hr (approximately 1 mL/kg/hr). The working diagnosis was that the patient had developed a nephropathy secondary to ibuprofen use.

On the third day of admission, the patient developed a refractory hyperkalaemia with an increasing creatinine and was transferred to the local renal unit for RRT (see [Figure 29.2](#), arrow indicates the point at which RRT commenced). She had several episodes of large volume epistaxis requiring packed red cell transfusion. On day 5, once her haemoglobin level was stable, she underwent a renal biopsy.

She continued to receive RRT for the next few days. The histology of her renal biopsy showed a diffuse large B-cell lymphoma. A positron emission tomography (PET) computed tomography (CT) scan was performed. This showed lymphoma involving the kidneys, bones, nodal stations, muscles, ovaries, small bowel and thyroid. A magnetic resonance imaging (MRI) scan of the hip confirmed that her pain was secondary to significant bone marrow infiltration. The patient was commenced on chemotherapy and required haemodialysis for 21 days.

Final diagnosis: B-cell lymphoma presenting with renal failure.

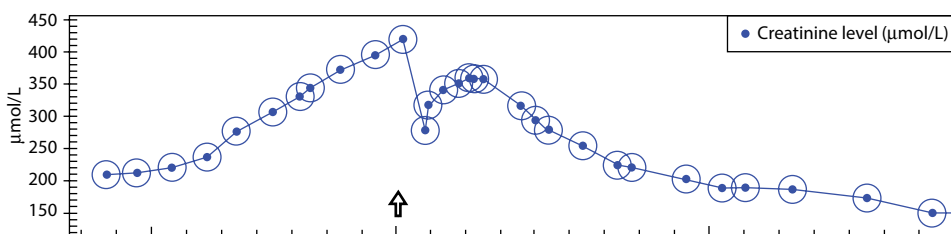
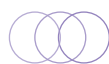


Figure 29.2 Creatinine levels over the course of the patient's admission. Note the reduction once renal replacement therapy was initiated (arrow).



OUTCOME

The patient had a protracted stay in hospital and developed complications including a severe pneumonia, a deep vein thrombosis and a pulmonary embolus. Post-chemotherapy, a repeat PET CT showed a very good response to treatment with complete resolution of previously abnormal tracer uptake in all nodal and extranodal sites with the exception of the kidneys and bony skeleton (likely to represent reactive tissue rather than residual disease). Her renal function has normalised. She is being followed up in clinic.

CASE DISCUSSION

This patient presented with epistaxis and bleeding from her gums, both of which are common problems in severe uraemia. There are multiple reasons why uraemia causes platelet dysfunction involving abnormal platelet–platelet and platelet–vessel wall interactions. High urea levels impair the synthesis of thromboxane A₂, which stimulates platelet activation and aggregation, as well as vasoconstriction. The production of prostaglandin-I₂ (prostacyclin), which inhibits platelet aggregation, is increased when high levels of urea are present. The production of von Willebrand factor polymers is also modified, resulting in prolonged bleeding times.

This case highlights the variety of ways in which lymphoma can present, with multi-system pathology although renal involvement is relatively uncommon. One retrospective study estimated that approximately 2% of patients with diffuse B-cell lymphoma have renal involvement.

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CASE 30: A SAUNA CLEANER WITH SHORTNESS OF BREATH

PATIENT HISTORY

A 26-year-old man presented to the emergency department with chest tightness and shortness of breath. He had noticed that he was becoming increasingly dyspnoeic over the preceding 3–4 weeks and was now short of breath on minimal exertion. He described his chest as feeling tight but denied pain. He had a non-productive cough and said that he had noticed a wheeze when he was particularly breathless. He denied any past medical history and took no regular medications. He worked as a cleaner in a local sauna. The patient had been born in the United Kingdom and had no known tuberculosis contacts. He lived with his brother and had one regular female sexual partner. He had never smoked tobacco. He drank around 30 units of alcohol per week and used ecstasy on weekends. He had travelled to Ibiza 2 months earlier.

EXAMINATION

Initial observations: T 36.8°C, HR 80 bpm, BP 140/70 mm Hg, RR 26 and SpO₂ 90% on room air (SpO₂ 84% on room air when the patient mobilised).

The patient appeared comfortable at rest but became short of breath when mobilising to the trolley to be examined. Fine inspiratory and expiratory crackles were heard in all lung fields on auscultation. There was no wheeze. His heart sounds were normal and he appeared euvolaemic. His abdomen was soft and non-tender.

INITIAL RESULTS

Routine bloods: WCC 9.9, N° 7.2, L° 1.4, E° 0.4, Hb 14, Plt 442, Na 143, K 4.5, Creat 88, CRP 8.

Arterial blood gas performed on room air: pH 7.42, pO₂ 8.2, pCO₂ 4.5, HCO₃ 24.5, BE 1.2, Lac 1.3.

DIFFERENTIAL DIAGNOSES

Although the patient is afebrile with no significant elevation in inflammatory markers, the onset of his dyspnoea and cough and the fact that he has no other past medical history makes community-acquired pneumonia the most probable diagnosis. Atypical infections, such as mycoplasma and legionella, should be considered.

Pneumocystis jirovecii pneumonia (PCP) produces symptoms of dyspnoea that develop gradually over several weeks with signs of bilateral consolidation on the chest x-ray. Patients are classically described as being significantly more hypoxic than one would expect from observing their respiratory rate (RR) and comfort at rest. *Pneumocystis jirovecii* is an opportunistic infection, primarily affecting immunosuppressed patients.

The patient may have undiagnosed asthma and is now presenting with his first exacerbation with a superadded infection. No wheeze was heard on auscultation of the chest, but the patient described feeling wheezy prior to admission.

Pulmonary sarcoidosis is another possible diagnosis. Patients typically present with progressive breathlessness and cough as well as fever and general malaise. They may describe arthralgia, uveitis and occasionally have a history of erythema nodsum or lupus pernio. A chest x-ray may show bihilar lymphadenopathy. The disease occurs more frequently in Afro-Caribbean patients.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient should be given oxygen therapy at the lowest concentration that maintains his SpO_2 at $\geq 94\%$. An urgent chest x-ray should be performed to identify possible consolidation or signs of fluid overload.

If he can produce sputum, this should be sent to the lab for microscopy and culture. Consider starting broad-spectrum antibiotics to treat community-acquired pneumonia. Blood and urine should be sent to detect possible mycoplasma and legionella antigens. An HIV test should be performed. In some centres, this can be performed rapidly, with results obtained via point of care testing within an hour. If the HIV test is positive, consider starting treatment for possible PCP.

CASE PROGRESSION

The patient required FiO_2 0.35 to maintain oxygen saturations of more than 94%, giving him a pO_2 of 10.3 on a repeat arterial blood gas. A chest x-ray was performed in the emergency department, showing bilateral lung field shadowing, which was more prominent on the right side. He was initially managed as a presumed community-acquired pneumonia with intravenous antibiotics (co-amoxiclav and doxycycline) for 24 hours, followed by a course of oral antibiotics. An HIV test was negative.

The patient remained hypoxic with no improvement in his condition. A computed tomography (CT) scan of his chest was performed, showing severe ground glass changes throughout both lungs (see [Figure 30.1](#)). A bronchoscopy was arranged for the following day. Samples from the bronchoalveolar lavage were sent for microscopy and culture. The acid-fast bacilli (AFB) smear showed no acid-fast bacilli.

The respiratory team reviewed the patient and diagnosed a likely hypersensitivity pneumonitis, presumably secondary to infection with *Mycobacterium avium complex*. Corticosteroid

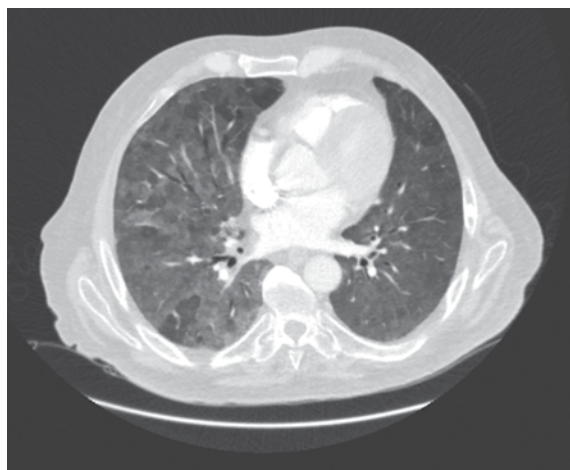
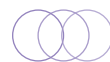


Figure 30.1 CT chest scan showing widespread ground glass changes.



therapy was commenced and the patient's symptoms gradually improved over the next 4 days. His hypoxia resolved and he was discharged home to complete a 3-week reducing course of prednisolone.

He was followed up in the respiratory clinic as an outpatient 2 weeks later. At this point, his bronchoalveolar lavage acid-fast bacillus culture had grown *Mycobacterium avium-intracellulare*.

Final diagnosis: *Mycobacterium avium* complex infection, also known as 'hot tub lung', probably acquired due to his work at the sauna.

OUTCOME

The patient left his job in the sauna shortly after being discharged from hospital. He initially required several courses of corticosteroids following his diagnosis but has now been well for over 18 months. A repeat chest x-ray showed complete resolution of the bilateral shadowing.

Two regular clients at the same sauna have since presented to the respiratory clinic with proven *Mycobacterium avium* complex infection. Both patients were of no fixed abode and were essentially residing at the sauna. The Health Protection Agency was notified regarding all three cases.

CASE DISCUSSION

Mycobacterium avium complex is a non-tuberculous mycobacterial pathogen that is ubiquitous within the environment, particularly favouring water- or soil-based environments. The bacteria are hydrophobic and able to survive exposure to high temperatures. Aerosolised *Mycobacterium avium* complex in water droplets are inhaled or ingested and can cause a hypersensitivity pneumonitis in immunocompromised patients.

Over the past decade, an increasing number of immunocompetent patients have presented with hypersensitivity pneumonitis secondary to *Mycobacterium avium* complex. A common feature in these patients is regular use or exposure to indoor hot tubs and saunas. Discontinuing exposure to the hot tubs, along with a course of corticosteroids, typically results in complete resolution of symptoms and radiological signs of infection.

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CASE 31: RECURRENT EPISODES OF ACUTE KIDNEY INJURY

PATIENT HISTORY

A 68-year-old man presented to the emergency department following an episode of collapse at home. He described a 4-day history of diarrhoea and vomiting. The diarrhoea was pale and watery with copious amounts of mucus. There was no fresh or altered blood in the stool. He was unable to quantify how frequently he was opening his bowels, responding with, 'constantly', whenever he was asked. He had been vomiting two to three times daily, usually after eating. He had been feeling light-headed for several hours until he lost consciousness upon standing. He awoke on the floor, feeling generally unwell but without any evidence of tongue biting or incontinence. His past medical history included type 2 diabetes mellitus, hypertension and hypercholesterolaemia. On direct questioning, he reported being constipated over recent weeks but had not used laxatives for this. He took 40 mg gliclazide BD and 20 mg simvastatin ON. He was a retired plumber and lived with his son. He was a current smoker of 10 cigarettes daily and had accumulated a 50 pack year history. He denied drinking alcohol or using recreational or herbal drugs. He had not travelled abroad for more than 5 years.

EXAMINATION

Initial observations: T 36.1°C, HR 96 bpm, BP 82/54 mm Hg, RR 18 and SpO₂ 97% on room air.

The patient appeared pale and fatigued. His mucus membranes were dry and his tongue was coated. He felt cool peripherally. His heart sounds were normal, his jugular venous pressure (JVP) was not visible and there was no peripheral oedema. His abdomen was soft but generally tender. Bowel sounds were active and of normal pitch. Digital rectal examination found colourless mucus within the rectum but no palpable masses. The patient was witnessed passing around 200 mL mucus per rectum during the clerking.

INITIAL RESULTS

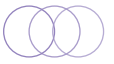
Routine blood tests: WCC 8.2, Hb 118, Plt 156, Na 124, K 4.4, Creat 576, CRP 10.

Venous blood gas: pH 7.31, HCO₃ 22.8, BE 5.9, Lac 2.9.

Capillary glucose level: 30.8 mmol/L.

DIFFERENTIAL DIAGNOSES

The patient has presented with a severe acute kidney injury following a 4-day history of copious diarrhoea with some vomiting. Given the abrupt onset of symptoms, gastroenteritis is the most likely diagnosis. When taking a history from this patient you will need to establish what



he had eaten in the 24 hours preceding onset of symptoms, such as undercooked poultry or food that had not been stored appropriately, leading to a bacterial gastroenteritis (including *Bacillus*, *Salmonella*, *Shigella* and *Campylobacter* species). If he has recently had a course of antibiotics then *Clostridium difficile* infection may be a possibility. Viral gastroenteritis, such as norovirus or rotavirus, may also be likely, particularly if the patient has been in contact with people who have similar symptoms. Viral colitis due to cytomegalovirus can occur but typically in association with immunosuppression.

This could represent a first presentation of inflammatory bowel disease (IBD), with both Crohn's disease and ulcerative colitis being possible diagnoses. IBD has a bimodal distribution in age of onset, with patients tending to present either in their teenage and early adult years or from the age of 50 to 70 years.

The patient described several weeks of constipation preceding the diarrhoea. Overflow diarrhoea is a possibility, but the symptoms have come on rather rapidly and are more severe than would be expected for this condition. The recent change in bowel habit is more suggestive of lower gastrointestinal tract malignancy. The vomiting and abdominal pain may be due to bowel obstruction caused by a neoplasm.

Diabetic gastroparesis occurs when persistently elevated glucose levels lead to autonomic neuropathy with vagus nerve involvement. Gastric emptying is delayed and patients may vomit frequently. Slower gastric transit time leads to increased bacterial replication and can result in small bowel bacterial overgrowth, causing diarrhoea and gastrointestinal tract obstruction. Masses of undigested food, known as bezoars, may form – these can also cause obstruction.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient has a severe acute kidney injury and appears dehydrated. He will need intravenous fluid rehydration with careful monitoring of his electrolytes and urea level. Rapid shifts in serum tonicity can cause central pontine myelinolysis and you should therefore aim to increase serum sodium levels by no more than 8–12 mmol/L in 24 hours. A urinary catheter should be inserted to allow accurate fluid input and output to be recorded. Given the degree of kidney injury with the possible need for renal replacement therapy (RRT), a high dependency unit setting may be a more appropriate place to monitor the patient, at least initially. An ultrasound scan of the kidneys should be performed to identify any possible obstructive lesions.

With regard to the symptoms of diarrhoea and vomiting, an abdominal x-ray should be performed, looking for a dilated bowel, indicative of obstruction. Stool should be sent for microscopy, culture and sensitivities. If the history is suggestive of possible *Clostridium difficile* or norovirus then stool should also be tested for these infections.

A stool chart should be commenced to document the frequency, colour and consistency of the bowel motions. Antibiotics, such as co-amoxiclav or cefuroxime and metronidazole should be started for a presumed gastroenteritis. A sigmoidoscopy will need to be performed at a later stage, once the acute kidney injury has started to resolve and the patient is stable.

The patient has an elevated blood glucose level. While he is acutely unwell an insulin sliding scale should be commenced.

CASE PROGRESSION

The patient was treated with intravenous 0.9% saline and a course of co-amoxiclav. An abdominal x-ray showed a small degree of faecal loading in the ascending colon but no signs of obstruction. A renal ultrasound scan showed bilateral echogenic kidneys consistent with acute tubular necrosis. The patient's renal function returned to baseline over the next 3 days. His diarrhoea settled completely and he was discharged home. His bloods at this time showed a sodium level of 137 mmol/L, a urea level of 7 mmol/L and a creatinine level of 75 $\mu\text{mol/L}$.

He re-presented to hospital 1 week later (visit 2) with further diarrhoea and another acute kidney injury (sodium 116 mmol/L, urea 90 mmol/L and creatinine 826 $\mu\text{mol/L}$). Stool samples showed no bacterial growth and were negative for norovirus. Again, he demonstrated what appeared to be a complete recovery within 48 hours and was discharged home with outpatient follow-up to consider the need for a sigmoidoscopy or colonoscopy.

In the outpatient clinic, the patient felt well and declined further investigations. The assumption was that an episode of gastroenteritis had occurred.

Approximately 6 months later, the patient was brought to the emergency department collapsed and hypotensive (visit 3). Once again, a history of profuse diarrhoea with abdominal pain was established and blood tests showed a moderate hyponatraemia and severe acute kidney injury. On this occasion, a flexible sigmoidoscopy was performed, which was reported to be normal. The working diagnosis was autonomic dysfunction with gastroparesis secondary to poor diabetic control. Gastric transit testing was scheduled.

The patient re-presented to hospital 2 weeks later with identical symptoms (visit 4). On this occasion, a *Campylobacter* species was isolated in the stool and the patient received antibiotic therapy for this. When he returned 2 weeks later (visit 5) with a creatinine level of 957 $\mu\text{mol/L}$, he was re-treated for presumed partially treated *Campylobacter* gastroenteritis. The sigmoidoscopy was repeated and again identified no abnormalities. (See [Figure 31.1](#)

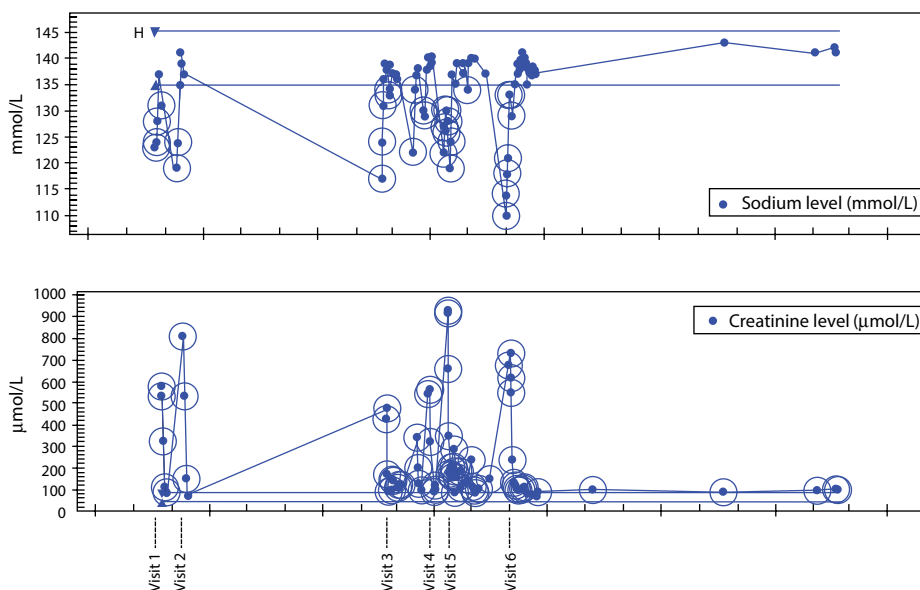


Figure 31.1 Sodium and creatinine levels at each presentation.



showing the creatinine and sodium levels of the patient during his time in hospital.) Note the severe acute kidney injury with hyponatraemia that resolves completely within 2–3 days, followed by another relapse several days or weeks later.

Four weeks later, the patient returned to hospital (visit 6). On this occasion, the sodium level had fallen to 107 mmol/L, the urea level was 84 mmol/L and the creatinine level was 794 μ mol/L. A blood gas showed a pH of 7.3 and a lactate level of 4.3 mmol/L. Again, he recovered within 2–3 days. During this admission, a colonoscopy was performed. This found a large, 8 cm carpeting lesion, starting at dentate line at 2 cm from the anal verge, that appeared almost circumferential. No areas of puckering, tethering or infiltration were seen.

Histology from the biopsies identified a tubular villous adenoma with low-grade dysplasia.

Final diagnosis: Tubular villous adenoma causing secretory diarrhoea.

OUTCOME

A magnetic resonance imaging (MRI) scan of the pelvis showed no invasion beyond the rectal wall. A staging computed tomography (CT) scan of the chest, abdomen and pelvis found no metastases. The patient initially declined surgery despite multiple attempts to persuade him of the necessity. Following several further admissions to another hospital, he opted to undergo surgical removal of the lesion. A low anterior resection with mucosectomy and colo-anal anastomosis was performed and the patient has remained well since. Reversal of the procedure is now being considered.

CASE DISCUSSION

Although an uncommon occurrence, it is well documented that rectal villous adenomas can cause secretory diarrhoea with water and electrolyte hypersecretion. This is sometimes referred to as McKittrick-Wheelock syndrome.

The diagnosis can be challenging to make and is often delayed. In order to develop such a severe acute kidney injury over the course of hours to days, the patient must be losing several litres of water daily per rectum. In this case, the adenoma was not visualised until the third endoscopy was performed. It is not clear why the patient initially appeared to have a 6-month period of remission between his second and third presentations.

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CASE 32: A FARMER WITH ABDOMINAL PAIN

PATIENT HISTORY

A 57-year-old man presented to hospital complaining of right-sided abdominal pain and vomiting. His symptoms had come on gradually 8 months earlier and had been gradually worsening. He felt nauseated for most of the day and often vomited after meals. He described a sensation of early satiety and a dull pain over the right side of his abdomen on eating or coughing. He had unintentionally lost around 10 kg of weight over 6 months. His past medical history included an episode of alcoholic hepatitis 10 years earlier. He took no regular medications. He worked as a farmer in New Zealand and had lived there for the past 35 years. He had returned to the United Kingdom 2 weeks earlier. He did not drink alcohol at present but had a past history of alcohol misuse. He did not smoke tobacco or use recreational drugs. He had no recent sexual partners.

EXAMINATION

Initial observations: T 37.3°C, HR 60 bpm, BP 108/68 mm Hg, RR 16, SpO₂ 99% on room air.

The patient appeared icteric and cachectic. His heart sounds were normal and he was euvolaemic. His chest was clear to auscultation. His abdomen was soft throughout with mild tenderness around the right upper quadrant. A firm, non-pulsatile, non-tender mass was palpated in the epigastric region, which was distinct from the liver and overlying soft tissues. There was no palpable hepatomegaly. There were no stigmata of chronic liver disease. There was no cervical, axillary or inguinal lymphadenopathy.

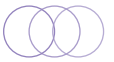
INITIAL RESULTS

Routine blood tests: WCC 10.2, N^o 4.6, L^o 2.3, E^o 2.8, Hb 104, Plt 199, Na 136, K 3.8, Creat 56, Bili 78, ALT 445, ALP 210, CRP 24, INR 1.4.

DIFFERENTIAL DIAGNOSES

The patient presents with an insidious onset of jaundice, weight loss and mild abdominal pain. The palpable mass in the abdomen may be the gallbladder. In calculous cholecystitis, the gallbladder may be enlarged and tense acutely but if chronic cholecystitis develops, it can become fibrosed rather than enlarged. In acalculous cholecystitis, the gallbladder is enlarged but very tender on palpation. If the mass is the gallbladder then obstruction of the biliary tree is more likely. Pancreatic adenocarcinoma, causing biliary compression is the most important pathology to exclude, given its poor prognosis. A pancreatic pseudocyst is another possibility.

The mass could represent a gastric neoplasm. This can cause jaundice due to biliary compression or because of hepatic metastases. Gastric cancers are most commonly adenocarcinomas



(90%–95%). Other cancers include lymphomas, gastrointestinal stromal tumours and carcinoid tumours.

Another important differential diagnosis is retroperitoneal lymphadenopathy. Causes for this can include lymphoma, HIV and tuberculosis infections, as well as gastric malignancy.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient describes nausea and occasional vomiting. Anti-emetics should be given as required and if he is not tolerating oral fluids then intravenous fluids will need to be administered. Analgesia should also be offered for his abdominal pain.

Malignant disease is at the top of the list of differential diagnoses. An abdominal ultrasound scan may further identify the palpable mass, but, ultimately, a computed tomography (CT) scan of the chest, abdomen and pelvis is likely to be required to identify a potential primary malignancy and any metastatic spread.

HIV serology should be sent and you should continue to monitor the patient's liver function tests and INR.

CASE PROGRESSION

A CT scan of the patient's chest, abdomen and pelvis was performed. This identified multiple cystic lesions within the liver, some of which had calcified (see [Figure 32.1](#), arrow points to lesion). Adjacent to the tail of the pancreas, there was a 1.3 cm cystic lesion. There was a paraduodenal cystic lesion measuring 6×5.5 cm lying immediately adjacent to the right of the head of the pancreas (see [Figure 32.2](#), arrow points to lesion). There was marked distension of the stomach, which was largely fluid filled. There was a further small 1.7 cm cyst lying adjacent to the second part of the duodenum. The region of D1/D2 appeared mildly thickened with a small amount of abnormal soft tissue at this site.



Figure 32.1 CT scan of the abdomen. The arrow shows a calcified cystic lesion within the liver.

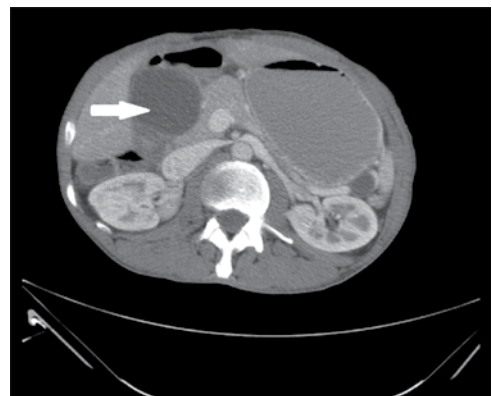


Figure 32.2 CT abdomen scan; the arrow shows a paraduodenal cystic lesion.



A CT-guided biopsy of one of the paraduodenal lesions was arranged. This showed altered blood, accompanying white blood cells with a mild increase in eosinophils. Microscopy from the cyst subsequently identified a protoscolex of *Echinococcus granulosus* and multiple parasite hooklets. No malignant cells were identified. *Echinococcus* serology was positive.

The patient underwent an oesophago-gastro-duodenoscopy, which showed extrinsic compression of the duodenum. A course of albendazole and praziquantel was commenced.

Final diagnosis: Hydatid disease with hepatic and extra-hepatic involvement leading to pancreatic and gastric outflow obstruction.

OUTCOME

The patient had a further CT scan of his abdomen 3 months later. This showed markedly fewer hepatic cysts, the majority of which had reduced in size. The paraduodenal cyst had reduced to 2.8×3 cm, but features of gastric outflow obstruction remained. The patient was readmitted to hospital for an elective laparotomy where the paraduodenal cyst was removed. He made a good recovery and his symptoms of nausea, vomiting and abdominal pain have completely resolved.

CASE DISCUSSION

Hydatid disease or echinococcosis is a parasitic infection of the *Echinococcus* tapeworm. The parasite's lifecycle is typically carried out between dog and sheep hosts. Adult tapeworms inhabit the gastrointestinal tract of dogs and their eggs are thus excreted via the faeces of the dog host. Grazing sheep ingest the eggs that subsequently develop into larval cysts. The cysts contain protoscolices, which have formed via asexual replication. Dogs that ingest meat from infected sheep will be exposed to the protoscolices. The protoscolices attach to the canine intestinal wall and mature into adult tapeworms.

This patient spent the majority of his adult life working as a farmer where he handled both dogs and sheep daily. His echinococcus infection is perhaps not surprising, but the severity of the infection is unusual. Cysts can develop in most human organs, with the liver, followed by the lungs being the most frequent site of infection. Cyst drainage, surgical resection and a course of the anthelmintic drug, albendazole, form the mainstay of treatment. Recently, combination therapy with albendazole and praziquantel, has demonstrated increased efficacy in the treatment of echinococcosis compared with albendazole monotherapy.

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CASE 33: SEVERE SEPSIS FOLLOWING TONSILLITIS

PATIENT HISTORY

A 22-year-old man presented to the emergency department complaining of a painful throat and swelling of the glands in his neck. He described a 5-day history of worsening odynophagia, fever and coryzal symptoms. He had visited his general practitioner and received a course of penicillin V 3 days earlier, but his symptoms had not improved. The odynophagia had become increasingly severe and he was now unable to swallow soft food. He felt nauseated and complained of malaise. He had no rash and denied symptoms of headache or photophobia. He had noticed cervical lymphadenopathy since the onset of his illness, predominantly affecting the left-side of his neck. His past medical history included three episodes of tonsillitis, each approximately 1 year apart. He took no regular medications aside from the recently prescribed penicillin V. He lived with his parents and sister, all of whom were well. He worked as an office clerk and had not travelled abroad for 2 years. He had never smoked tobacco and drank around 20 units of alcohol per week. He used both cocaine and marijuana at weekends.

EXAMINATION

Initial observations: T 39.7°C, HR 108 bpm, BP 128/84 mm Hg, RR 20, SpO₂ 100% on room air.

On examination, the patient appeared unwell and diaphoretic. His mucus membranes were dry. His chest was clear to auscultation. His heart sounds were normal and there was no peripheral oedema. His abdomen was soft and mildly tender throughout. His pharynx was erythematous with visible exudate on both tonsils. There was left-sided cervical lymphadenopathy – his submandibular lymph nodes measured up to 1.5 cm and were soft and tender on palpation.

INITIAL RESULTS

Routine blood tests: WCC 24.7, N° 22.1, L° 2.4, Hb 148, Plt 560, Na 132, K 4.8, Urea 17.2, Creat 92, Bili 28, ALT 39, ALP 81, INR 1.1, CRP 423.

DIFFERENTIAL DIAGNOSES

Viral infection, with adenovirus, rhinovirus or influenza, is the most common cause of tonsillitis. Secondary bacterial infection can subsequently occur. Alternatively, the patient may have a bacterial infection, usually caused by group A β -haemolytic streptococcus or, less commonly, *Staphylococcus aureus*.

A peritonsillar abscess, or quinsy, may develop around the peritonsillar space. Aside from pain and lymphadenopathy, patients are at risk of severe sepsis. The abscess can extend to cause airway compression.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient is dehydrated and needs intravenous fluid rehydration. In this case, either 0.9% saline or Hartmann's solution would be appropriate. His urine output should be monitored to guide ongoing fluid rehydration.

A septic screen should be performed – the patient will need to have blood cultures taken, as well as swabs of his throat. A chest x-ray and urine dip should be carried out. Blood tests should be sent for Epstein–Barr virus (EBV), cytomegalovirus and a Paul–Bunnell or Monospot test. An anti-streptolysin O titre should also be sent. A lactate dehydrogenase level is a non-specific marker of high cell turnover and if very elevated, can be indicative of conditions such as lymphoma.

If the patient does not improve over the first few hours of admission, the ear, nose and throat (ENT) team should review the patient regarding a possible peri-tonsillar abscess to allow early surgical intervention with incision and drainage of pus.

CASE PROGRESSION

The patient was admitted for intravenous antibiotics. He was treated initially with co-amoxiclav and gentamicin. He remained febrile, with temperatures of 39–40°C. His chest x-ray was unremarkable. After 24 hours of treatment, his inflammatory markers were rising and he was hypotensive despite intravenous fluids.

Toward the end of his second day of admission, he was becoming increasingly short of breath and complaining of difficulty swallowing fluids. On listening to his chest, crackles were heard throughout the mid and lower zones bilaterally. The lymphadenopathy around the left anterior cervical region appeared more prominent. A mobile chest x-ray showed new perihilar consolidation and signs of fluid overload. The decision was made to electively intubate the patient on the ward in case of further deterioration. He was taken to the intensive care unit where he received inotropic support.

He developed an acute hepatitis and the nurse caring for the patient identified swelling of the metacarpophalangeal joints of the left third and fourth digits. A computed tomography (CT) scan of his chest showed multifocal areas of consolidation and ill-defined nodular opacities measuring 1–2 cm in size within the visualised parenchyma. There were moderate bilateral pleural effusions. There was significant mediastinal lymphadenopathy. Overall, the picture was in keeping with a clinical diagnosis of septic emboli to the lungs. Interestingly, the left internal jugular vein appeared unenhanced, suspicious for thrombosis. (See [Figure 33.1](#) – arrow 1 points to left internal jugular vein where minimal contrast is seen, indicative of occlusion, while arrow 2 points to right internal jugular vein which enhances due to contrast flow.)

Left internal jugular vein thrombosis was confirmed with a Doppler ultrasound scan. (See [Figure 33.2](#) – arrow 1 points to the left carotid artery and arrow 2 points to the left internal jugular vein where there is minimal flow.) Low molecular weight heparin treatment was commenced. At this stage, the blood cultures had isolated *Fusobacterium necrophorum* with full sensitivity to metronidazole. His antibiotic therapy was modified accordingly.

Final diagnosis: Lemierre's syndrome.

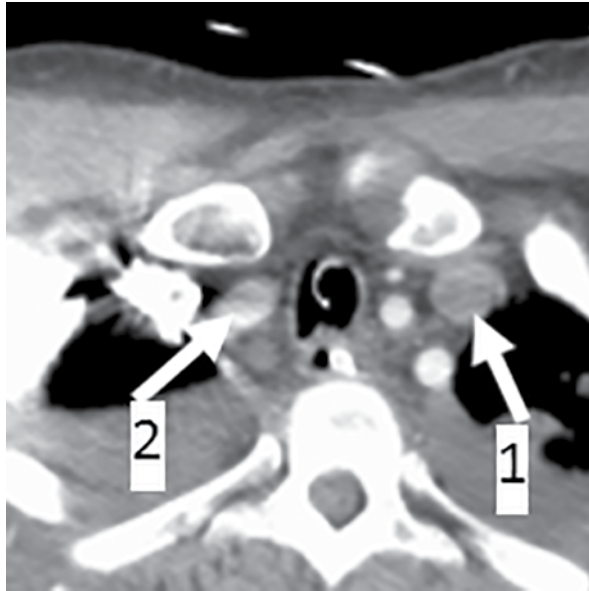


Figure 33.1 CT scan showing minimal contrast passing through the left internal jugular vein (arrow 1), with normal enhancement of the right internal jugular vein (arrow 2).

OUTCOME

The patient made a slow recovery over the next fortnight. He was eventually discharged after 4 weeks of care as an inpatient to complete 6 months of anti-coagulation therapy with warfarin. He remains well in the community.

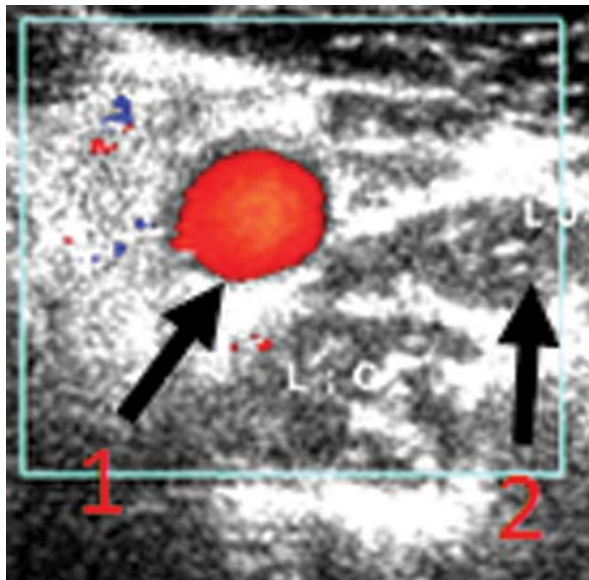
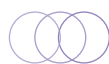


Figure 33.2 Doppler ultrasound scan.



CASE DISCUSSION

Lemierre's syndrome is an eponymous term for thrombophlebitis of the internal jugular vein. This classically occurs following an episode of pharyngitis or tonsillitis where a peritonsillar abscess forms. Anaerobic bacteria, often *Fusobacterium necrophorum*, reproduce within the abscess and invade the nearby structures, leading to thrombophlebitis of the internal jugular vein.

Severe sepsis from Lemierre's syndrome often results in complications such as pulmonary emboli, hepatitis and meningitis. Antibiotic therapy usually centres on beta-lactamase penicillins with clavulanic acid and metronidazole.

Thrombosis of the internal jugular vein is ideally treated with an intravenous heparin infusion in the acute stage of illness, followed by several months of oral anticoagulation agents, depending on the coagulation status and bleeding risk of the patient.

Although Lemierre's syndrome is uncommon, it is associated with a very high morbidity and mortality. Doctors should have a high index of suspicion for this condition in patients who present with evidence of a peritonsillar abscess and sepsis.

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CASE 34: AN ELDERLY MAN WITH CONFUSION

CASE HISTORY

A 73-year-old man was brought to hospital by a friend who felt that he had become increasingly confused over the preceding 4–5 weeks. The patient described a generalised sense of disorientation and difficulty remembering how to perform simple activities such as dressing himself. He was becoming progressively more unsteady when walking and had fallen several times over recent days. Of note, he had fallen 6 weeks earlier and sustained a head injury while travelling on a train. His past medical history included juvenile myoclonic epilepsy. He took 500 mg sodium valproate BD and primidone 250 mg BD. He was a retired history teacher who lived alone and was usually independent with activities of daily living. He had never smoked tobacco and did not drink alcohol.

EXAMINATION

Initial observations: T 36.9°C, HR 76 bpm, BP 119/71 mm Hg, RR 16 and SpO₂ 98% on room air.

The patient was alert but clearly confused. He achieved an abbreviated mental test score of 3 out of 10 (points gained for recall, recognition and orientation to place). His chest was clear to auscultation. He had dual heart sounds with no murmurs and appeared euvolaemic. Neurological examination identified a small, reactive left pupil (size 2) and a dilated, poorly responsive right pupil (size 7) that was deviated toward the right. He had marked horizontal left-beating nystagmus. He was dysarthric and apraxic with an ataxic gait.

INITIAL RESULTS

Initial blood tests: WCC 6.6, Hb 126, Plt 201, Na 135, K 4.1, Creat 46, CRP 29.

DIFFERENTIAL DIAGNOSES

The patient demonstrates several neurological signs that would not be in keeping with a single lesion. He has had several falls recently, any one of which may have resulted in a head injury. Interestingly, the patient fell while on a train at least a week prior to his friend noticing the confusion and unsteadiness. This may have been part of an underlying pathology or it may be that the patient has had a large subdural bleed following the initial fall that has resulted in ongoing neurological impairment due to compression from a haematoma. A subarachnoid bleed could have caused the initial fall and the resulting haematoma may be responsible for the current symptoms.

An encephalitic process, such as viral or autoimmune encephalitis, can cause cognitive impairment and widespread neurological change. Limbic encephalitis, for example, may present with impairment of memory function and motor function. A fever and elevated inflammatory markers would be expected but are not always present in cases of viral encephalitis.

The autoimmune encephalitides may be associated with an underlying malignancy as part of a paraneoplastic syndrome.

Creutzfeldt–Jakob disease occurs due to the deposition of abnormal proteins, known as prions, which cause neurodegeneration. Patients present with a rapidly progressive dementia, displaying memory loss and psychiatric symptoms.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The first step would be to perform a computed tomography (CT) scan of the head (ideally with contrast), looking for evidence of a bleed, space-occupying lesion or abnormal enhancement. If the CT scan is normal, a magnetic resonance imaging (MRI) scan of the brain should be performed to further investigate for subtle pathological changes.

Depending on the results of the imaging studies, a lumbar puncture should be considered, providing there is no evidence of raised intracranial pressure (ICP). Cerebrospinal fluid (CSF) samples should be sent for virology, voltage-gated potassium channel antibodies and autoimmune antibodies (*N*-methyl-D-aspartate [NMDA] receptor and glutamic acid decarboxylase [GAD] antibodies).

CASE PROGRESSION

A CT head scan showed that the brain was grossly abnormal with oedema and white matter abnormality (see [Figure 34.1](#)). A focus of left parietal subarachnoid haemorrhage was present. The neurology team reviewed and advised that the findings may represent a paraneoplastic leukoencephalopathy.

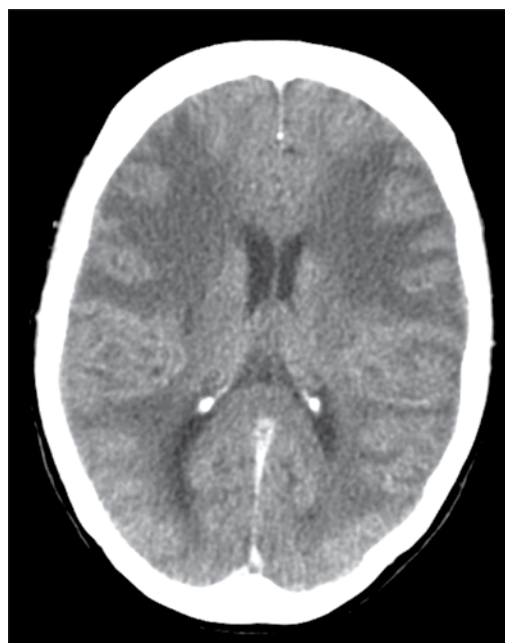
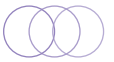


Figure 34.1 CT brain scan.



An MRI brain scan showed striking appearances with bilateral extensive white matter change and oedema throughout both hemispheres and petechial haemorrhages (see [Figure 34.2](#)).

A CT positron emission tomography (PET) scan was performed to investigate for underlying malignancy, but there was no abnormal tracer uptake. A lumbar puncture was performed – no bacterial or viral infections were identified. Several autoimmune CSF tests were sent, but results were not expected for several weeks. The patient rapidly deteriorated over the next week, becoming bedbound with significant cognitive decline. He was no longer able to communicate verbally and was mumbling incoherently.

The CT and MRI images were reviewed by a consultant neuroradiologist who felt that this case could represent an extreme and unusual form of cerebral amyloid angiopathy and related leukoencephalopathy, having seen similar cases in the literature. The medical team commenced intravenous methylprednisolone to treat presumed cerebral amyloid angiopathy. A brain biopsy subsequently confirmed the diagnosis.

Final diagnosis: Cerebral amyloid angiopathy.

OUTCOME

The patient showed a dramatic improvement upon commencing corticosteroids. He was able to leave hospital several weeks later and is now living independently with good cognitive function. He has regular outpatient MRI scans and his corticosteroid dose is being gradually weaned.

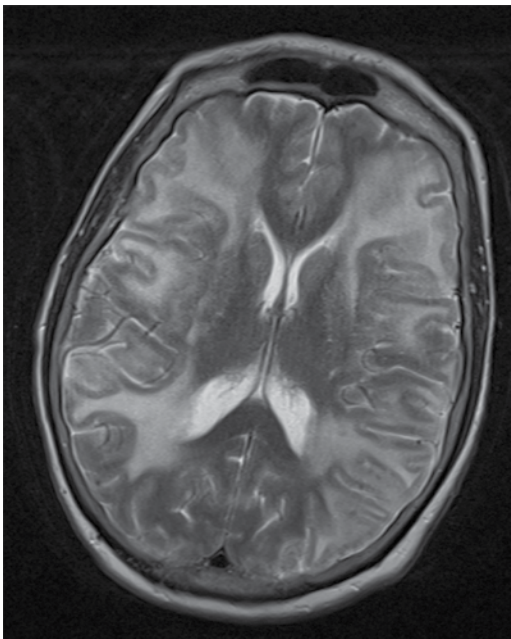
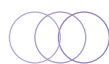


Figure 34.2 MRI brain scan.



CASE DISCUSSION

Amyloidosis is a term encompassing a number of conditions where insoluble amyloid proteins form deposits within tissues, resulting in disease. In cerebral amyloid angiopathy, fibrils of β -amyloid protein are deposited within the tunica media and adventitia of cerebral and leptomeningeal blood vessels. β -Amyloid may accumulate either due to processes causing increased production or because of impaired clearance by endocytosis. Cerebral amyloid angiopathy is not related to systemic amyloidosis. β -Amyloid deposition causes increased fragility of the vessels making them prone to haemorrhage.

Patients present with features of a vascular dementia, headaches, seizures or recurrent intracerebral bleeds. Cerebral amyloid angiopathy may be responsible for some of the white matter changes observed in Alzheimer's disease. There is currently no evidence-based treatment for cerebral amyloid angiopathy, although case reports have shown that a number of patients do respond to steroid treatment. This patient appears to have one of the steroid-responsive forms of the condition.

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CASE 35: NUMB FINGERS AND EOSINOPHILIA

PATIENT HISTORY

A 74-year-old man presented to the out-of-hours general practitioner in the emergency department with a 1-week history of numbness of his fingers. He had initially noticed occasional 'pins and needles' sensations in all 10 digits when he was using his hands, for example when chopping vegetables. Over the past few days, a progressive loss of sensation in the fingers had developed and he now complained of generalised weakness of the hands bilaterally. He denied any recent trauma. His past medical history included asthma diagnosed by his general practitioner 6 months earlier. His only medications were seretide and salbutamol inhalers and he denied use of over-the-counter or herbal drugs. Systems review identified a 2-week history of a cough productive of colourless sputum and shortness of breath on exertion. On direct questioning he admitted to approximately 10 kg of unintentional weight loss over the preceding 2 months and a feeling of general malaise. He was a retired tax inspector who lived alone. He had never smoked and drank no alcohol. He had not travelled abroad for more than 30 years.

EXAMINATION

Initial observations: T 36.5°C, HR 90 bpm, BP 114/71 mm Hg, RR 20 and SpO₂ 93% on room air.

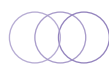
On examination, the patient appeared alert and comfortable at rest. On auscultation of his chest, there was a widespread, polyphonic wheeze audible throughout both lung fields on expiration. Cardiovascular and abdominal examinations were unremarkable. Cranial nerve examination identified no abnormalities. Upper limb examination revealed wasting of the thenar eminences bilaterally. There was reduced power (3/5) when wrist flexion, handgrip and thumb opposition were assessed. The biceps, triceps and brachioradialis reflexes were present with reinforcement. There was reduced sensation to light touch in the C3-C7 dermatomes. Proprioception and co-ordination were normal. There was a coarse resting tremor of the hands. Lower limb examination was unremarkable.

INITIAL RESULTS

Routine blood results: WCC 25.7, N^o 7.6, L^o 1.8, W^o 14.9, Hb 134, Plt 176, Na 136, K 4.5, Creat 77, cCa 2.29, CRP 36.

DIFFERENTIAL DIAGNOSES

There are several key points of this case that are worth considering when formulating a differential diagnosis. First, the patient has what appears to be bilateral high median nerve lesions that have apparently come on over the course of several days. We know the median nerve lesion is high, rather than low, because the patient has impaired finger and wrist flexion as well as loss of thumb opposition. Wasting of the thenar eminences suggests that the underlying



pathological process has been in place for significantly longer than a week. Bilateral lesions can be attributed to a congenital small carpal tunnels or bilateral trauma.

Osteophyte formation or an underlying arthritic process may cause bilateral neural compression. Repetitive strain injury is another possibility and history taking should focus on any change in activities, for example a new hobby or occupation, over the past few months.

New, rapid weight gain can cause bilateral nerve compression that develops simultaneously, although this patient reports weight loss. Along the same lines, acromegaly is a possibility and the physician who clerks this patient should ask whether they have noticed rings becoming tighter around the fingers, whether their glove or shoe size has increased and whether their facial features have recently become coarser. Infiltrative systemic conditions, such as sarcoidosis and amyloidosis are also possibilities.

The patient has a marked eosinophilia. Allergic and atopic responses, such as asthma, hay fever or drug reactions, are a common cause of eosinophilia. Of note, the patient has apparently received a diagnosis of asthma several months ago. It is extremely uncommon to develop asthma in older age. Chronic obstructive pulmonary disease would be a more likely diagnosis, but this patient has never smoked. Further history taking should identify whether the patient has ever had significant long-term exposure to tobacco smoke. It is also important to establish whether the patient has had lifelong symptoms of asthma but has only recently received the diagnosis, or whether his shortness of breath and wheeze truly began several months ago.

Eosinophilic granulomatosis with polyangiitis (EGPA, formerly Churg-Strauss syndrome) is a form of vasculitis affecting small- to medium-sized blood vessels. Patients present with symptoms of new-onset asthma or sinusitis and blood results typically show a marked eosinophilia. Development of polyneuropathy or mononeuritis multiplex is associated with this syndrome. This would provide a unifying diagnosis for all of the patient's symptoms.

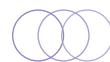
Patients may mount an eosinophilic response to parasitic infection, but this patient denied any travel history for more than 30 years. Some parasites may cause either a transient or chronic eosinophilic pneumonia (also known as Löffler's syndrome), which may be another explanation for this patient's relatively new onset of asthma symptoms. The lifecycle of the hookworms, *Ancylostoma duodenale* and *Necator americanus*, as well as *Strongyloides stercoralis* and *Ascaris lumbricoides* includes a stage of inhabiting the lungs as well as a stage where their eggs may travel to the lungs via haematogenous spread. Lung flukes and tapeworms may also invade the lungs.

Some malignancies, including myeloid and lymphoid neoplasms and chronic eosinophilic leukaemia may present with an eosinophilia. An underlying neoplastic process could also explain the patient's weight loss and malaise. If there was infiltration resulting in neural compression, this may explain the bilateral median nerve lesions.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient should have a chest x-ray to identify any underlying pathology that may be responsible for his symptoms of wheeze and loss of weight, such as an abnormal lung mass. A salbutamol nebuliser should be given as this may improve his wheeze. The patient has an SpO₂ of 93% on air. A blood gas sample should be obtained to monitor arterial oxygen and carbon dioxide levels.

A neurology team review should be arranged to assist with investigation into why the patient has developed acute, bilateral high median nerve palsies.



CASE PROGRESSION

The chest x-ray showed fine reticular changes within both lower zones. A computed tomography (CT) scan of the chest, abdomen and pelvis was subsequently performed to investigate for a possible malignancy. This showed multiple nodules seen throughout the lungs, which had a tree-in-bud appearance peripherally.

Blood was sent for IgE levels. These came back extremely elevated at >5000 KU/L (reference range 0–81 KU/L). A vasculitis screen identified that the patient's blood was positive for perinuclear anti-neutrophil cytoplasmic antibodies (p-ANCA) and also myeloperoxidase (MPO), consistent with an underlying vasculitis. The respiratory team diagnosed probable EGPA.

The eosinophil count continued to climb, reaching 20.7×10^9 by day. The neurology and rheumatology teams reviewed the patient regarding his upper limb symptoms. Electromyography and muscle and nerve biopsies confirmed bilateral, very severe high median nerve lesions, consistent with mononeuritis multiplex.

Pulsed intravenous methylprednisolone therapy was commenced and the patient demonstrated a good response.

Final diagnosis: EGPA with mononeuritis multiplex.

OUTCOME

The patient required several long-term courses of corticosteroids over the following year. He generally made a good recovery, although he did require several hospital admissions for management of asthma symptoms. His neuropathies have largely resolved.

CASE DISCUSSION

EGPA is a granulomatous vasculitis that causes a syndrome of allergic rhinitis, asthma, sinusitis, peripheral eosinophilia and mononeuritis multiplex. The diagnosis of asthma may precede other features of the vasculitis by many years.

Patients classically have elevated IgE levels and the majority are p-ANCA positive with anti-MPO antibodies.

Courses of corticosteroids form the mainstay of treatment when patients develop a flare of EGPA symptoms. Patients may require long-term corticosteroid therapy to prevent further exacerbations of the disease. In severe cases, treatment with cytotoxic agents such as cyclophosphamide and infliximab may be required.

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CASE 36: FEVER, WEIGHT LOSS AND NIGHT SWEATS

PATIENT HISTORY

A 27-year-old man was referred to the emergency department by his general practitioner (GP) to investigate a 6–8 week history of intermittent left-sided chest pain, fevers, night sweats and weight loss. The chest pain was pleuritic in nature and was generally present when the patient exerted himself. He had noticed fevers and chills throughout the day and was experiencing drenching night sweats when sleeping. The patient weighed himself regularly at his local gym and stated that he had unintentionally lost 18 kg weight in the preceding 6 weeks. He had also experienced lower back pain over the past 4 weeks and had tried multiple analgesic agents with minimal improvement. His past history included hypertension and depression. He took 5 mg amlodipine daily. He was Ghanaian and had come to the United Kingdom 20 years ago with no foreign travel since. He worked in a launderette and lived with his wife, who had suffered from tuberculosis in childhood. He had never smoked tobacco and denied regular consumption of alcohol or use of recreational drugs. His wife and colleagues were, to his knowledge, not experiencing similar symptoms.

EXAMINATION

Initial observations: T 37.9°C, HR 96 bpm, BP 113/66 mm Hg, RR 20 and SpO₂ 99% on room air.

The patient was alert and orientated. He appeared well, but felt hot to touch. His chest was clear to auscultation, but breath sounds were reduced at the left base. His heart sounds were dual and there was a loud diastolic murmur in the aortic region. Abdominal examination identified left and right upper quadrant tenderness. Neurological examination was unremarkable. There was point tenderness overlying the L4–S1 vertebrae.

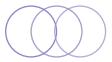
INITIAL RESULTS

Routine blood tests: WCC 13.1, N^o 9.7, L^o 0.5, Hb 97, Plt 255, Na 130, K 4.5, Creat 85, Bili 5, ALT 18, ALP 67, CRP 108.

DIFFERENTIAL DIAGNOSES

The patient's wife has a history of tuberculosis infection, and the patient has spent the majority of his life in Ghana and London, both of which have a high incidence of tuberculosis infection. The multiple examination findings could represent pulmonary tuberculosis with spread to the abdomen and bones (Pott disease). The history of fevers, night sweats and weight loss would support this diagnosis.

Infective endocarditis has to be high up on the list of differential diagnoses. The patient describes fevers, weight loss and night sweats and he has a diastolic heart murmur. While he has no obvious risk factors for infective endocarditis, such as intravenous drug use or recent dental surgery, this would provide a unifying diagnosis for his symptoms. Metastatic abscess



formation or septic emboli could explain his spinal and right upper quadrant abdominal tenderness. Septic emboli could have caused pulmonary infarction and the subsequent development of a reactive pleural effusion. Splenomegaly would explain the left upper quadrant abdominal tenderness.

Lymphoma with involvement of the left lung, liver and spine is another possibility. This could also cause the patient's constitutional symptoms. Lymphadenopathy would be expected, but the initial clerking does not specify whether this was examined for. Hodgkin's lymphoma typically affects patients in second and third decades of life. Non-Hodgkin's lymphoma and HIV-related lymphoma are possibilities.

Other malignancies with metastatic deposits should be considered. Given his young age, the patient is probably most at risk of testicular cancer. Testicular cancer most commonly causes metastases to lymph nodes in the abdomen but may also spread to involve the lungs, liver and bones.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

There is no documentation of examination for cervical, axillary or inguinal lymphadenopathy so this will need to be performed, in addition to a testicular examination. A full septic screen, including blood cultures and a chest x-ray should be performed to identify a potential focus of infection. If the patient can produce sputum then this should be sent for detection of acid fast bacilli as well as microscopy, culture and sensitivity. An HIV test should be performed.

While the patient remains well with no overt signs of sepsis, it is worth holding off antibiotic therapy until a likely source of infection has been identified.

An echocardiogram should be requested in view of the patient's heart murmur and an abdominal ultrasound scan should also be considered if the bilateral upper quadrant tenderness persists – this could represent hepatosplenomegaly that is difficult to palpate.

CASE PROGRESSION

A chest x-ray showed a small left-sided pleural effusion. The patient continued to spike low-grade fevers. Antibiotics were not given at this stage as the patient remained well and no clear source of infection had been identified. An HIV test was negative. Unfortunately, the blood cultures taken in the emergency department were misplaced and never arrived at the laboratory.

A computed tomography (CT) scan of the chest, abdomen and pelvis was performed to identify any foci of infection, including tuberculosis. This showed bilateral pleural effusions, plus multiple cysts in the liver and the spleen (see [Figure 36.1](#)). Some cysts were newly developed. There was also noted to be extensive sclerosis, cortical destruction and multiple rounded lytic lesions in the L5 and S1 vertebral bodies (see [Figure 36.2](#)).

An echocardiogram found a large, mobile vegetation attached to all cusps of the aortic valve creating a severe jet of aortic regurgitation. On inspection, the patient was noted to have one splinter haemorrhage on his thumb nail and conjunctival petechiae. Further history-taking elicited that the patient had undergone a tooth extraction 2 months prior to developing fevers and weight loss.

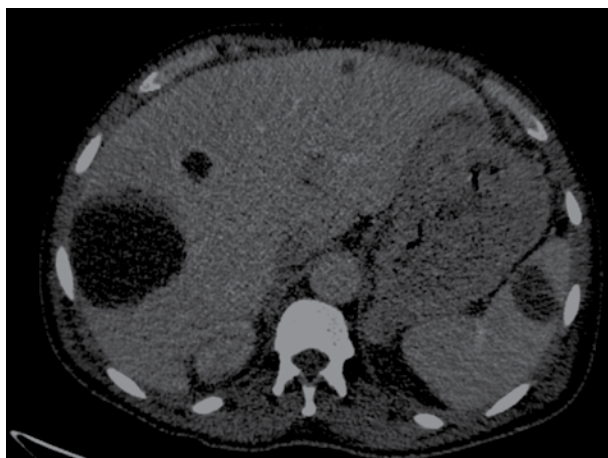


Figure 36.1 CT scan of the abdomen. Hepatic and splenic cystic lesions are present.

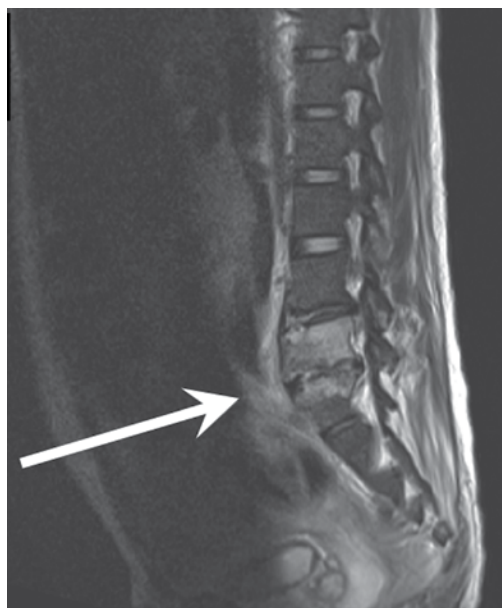
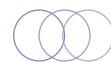


Figure 36.2 Lytic lesions within the L5 and S1 vertebral bodies.

Streptococcus sanguinis (*viridans*) was subsequently isolated from the aerobic and anaerobic bottles of all three sets of blood cultures taken on day 6 of admission.

Final diagnosis: Aortic valve streptococcal endocarditis with discitis and hepatic cysts.



OUTCOME

The patient underwent an aortic valve replacement and was treated with an extended course of antibiotics (80 mg gentamicin BD and 2.4 g benzylpenicillin 4 hourly). He has remained well in the community for the past 4 months.

CASE DISCUSSION

Streptococcal endocarditis is most commonly caused by dental procedures leading to *Streptococcus sanguinis*, which resides in the oral cavity, entering the bloodstream and colonising the heart valves. Benzylpenicillin and gentamicin form the mainstay of treatment.

This case highlights a number of ways in which we can improve the diagnosis and management of such patients. First, more focussed clerking at any stage of the admission could have identified the recent history of dental surgery, which the patient did not recall until the history was re-taken by a cardiologist. Second, the emergency department took blood cultures that were subsequently misplaced. The medical team did not repeat the cultures as they were awaiting the results of the initial cultures. When infective endocarditis is suspected, a minimum of three sets of blood cultures should be taken, at least 6 hours apart to aid isolation of the responsible organism.

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CASE 37: COLLAPSED IN THE CORRIDOR

PATIENT HISTORY

The hospital crash team was called to attend to a 23-year-old man who was found collapsed in a corridor outside the emergency department. He complained of feeling very fatigued and light-headed, and described his legs giving way. He had been advised to attend the department by his work colleagues who noticed that he had become progressively more unwell over a period of several days. He gave a 4–6 week history of anorexia and weight loss (estimated to be around 10 kg over 4 weeks). He attributed his reduced oral intake to vague abdominal discomfort and nausea. He had vomited two to three times over the last few days. He denied loose stools or constipation. On direct questioning, he admitted to two recent episodes of urinary incontinence, which he described as ‘not quite making it to the bathroom on time despite rushing there’. When asked if he had noticed that his urine was dark and his stools were pale, he admitted to very dark urine but was unsure regarding stool colour. He had no past medical history and took no regular medications. He was an office worker who lived alone and had one long-term female sexual partner. He drank 6–8 units of alcohol per week and neither smoked nor used recreational drugs. He had not travelled abroad in the past 1 year.

EXAMINATION

Initial observations: T 37°C, HR 98 bpm, BP 104/62 mm Hg, RR 18 and SpO₂ 100% on room air.

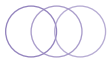
The patient was alert and orientated but appeared distressed. He was cachectic in appearance with an estimated body mass index of 16. Respiratory and cardiovascular examinations were unremarkable. Abdominal examination revealed a soft abdomen with a palpable 1 cm smooth liver edge and mild, generalised tenderness. Neurological examination identified bilaterally reduced power in the lower limbs (power 4/5). There was had no sensory loss, and in particular there was no saddle anaesthesia. There was no documentation of plantar reflexes or gait assessment.

INITIAL RESULTS

Routine blood tests (taken at scene of collapse): WCC 5.3, N° 4.4, L° 1.0, Hb 141, MCV 84, Plt 268, Na 140, K 4.0, Urea 13.0, Creat 77 (baseline 50), CRP 2.

DIFFERENTIAL DIAGNOSES

The patient describes a progressive, relatively chronic illness characterised by nausea, abdominal pain and weight loss. He is unsure whether his stools have been pale but certainly described dark urine – this could represent jaundice or possibly concentrated urine due to poor fluid intake. There is no description of yellow sclerae, pigmented skin or features of decompensated liver disease. The list for possible causes of chronic, progressive jaundice includes cancer, such as a primary or secondary hepatic malignancy, or a pancreatic or biliary tumour. The normal haemoglobin level and mean cell volume make haemolysis unlikely. A chronic inflammatory process, such as autoimmune hepatitis, or an infective cause such as



hepatitis B or C should also be considered. Liver function tests will need to be sent urgently, along with a coagulation screen (as the liver synthesises multiple coagulation factors).

A common cause of nausea, urinary frequency and weight loss is diabetes mellitus. This could be a new presentation of type 2 diabetes mellitus (T2DM) with hyperglycaemia or, possibly, a late presentation of type 1 diabetes mellitus. Latent Autoimmune Diabetes of Adulthood (LADA, also known as type 1.5 diabetes) should also be considered. A capillary glucose reading should be checked at the scene of the collapse, but a blood sample should also be sent to the laboratory to check the glucose level, as capillary glucose readings cover a narrow range, typically recording values above 30–33 mmol/L as 'High / Hi'.

Malignancy may be present, with common cancers in a patient of this age including testicular cancer and lymphoma. Examination of the patient's testicles and lymph nodes should be carried out once the patient can be reviewed in the emergency department or on a ward. The lower limb weakness and urinary frequency with loss of bladder control could represent spinal cord compression, due to metastases, although there was no saddle anaesthesia in the examination. There was no documentation of an anal tone assessment, which should also always be performed when cauda equina is suspected.

HOW WOULD YOU MANAGE THE PATIENT INITIALLY?

The patient should be moved to an area in either the emergency department or a medical ward where he can be fully assessed. The systems examination should be repeated to include a more thorough neurological examination, including cranial nerves, gait and anal tone, as well as testicular and lymph node examination.

The patient has a mild tachycardia and is hypotensive. An assessment of the patient's fluid status is important in this case – look at his jugular venous pressure and his ankles (for the presence of peripheral oedema) and comment on whether his mucous membranes are dry. If you suspect the patient is fluid deplete, commence intravenous fluid rehydration and advise the medical team to monitor his urine output. In this situation, 0.9% saline or compound sodium lactate (Hartmann's solution) would be appropriate.

Blood tests should be sent to check liver function, glucose level and, in view of his recent anorexia, electrolytes including calcium, phosphate and magnesium.

A chest x-ray (to look for possible malignancy or infection) and a urine dip (to identify infection, proteinuria, haematuria or glycosuria) should be performed. A venous blood gas sample should also be considered – the patient has impaired renal function and an underlying metabolic acidosis should therefore be excluded.

This patient is likely to require further investigations, either as an inpatient or outpatient, for possible causes of weight loss, which may include computed tomography (CT) imaging of the chest, abdomen and pelvis or endoscopies of the gastrointestinal tract.

CASE PROGRESSION

A full neurological examination identified proximal weakness of the upper and lower limbs, with shoulder abduction, shoulder adduction, shoulder flexion, hip flexion and hip extension all graded at 4/5 power. Blood results showed normal liver function. After 12 hours of



intravenous fluids, the patient's renal function normalised and his tachycardia and hypotension resolved. His capillary and blood glucose levels were checked several times and the results were consistently within the normal range.

An abdominal ultrasound noted that the intra-abdominal organs were of normal size with no obvious pathology. The patient continued to complain of nausea and abdominal pain, with little relief from simple analgesia or anti-emetics. His oral intake was poor and the dietitians arranged for the patient to commence nutritional supplementation and a high-calorie diet.

The ward team noticed that the patient seemed confused at times, with episodes of both anxiety and depressed affect. On the fifth day of his admission, he tried to smash a window and was transiently unaware of his surroundings. A CT scan of the brain was performed – this was unremarkable. A lumbar puncture was carried out to investigate for possible central nervous system infections, including viral encephalitis, but identified no abnormalities. Autoimmune encephalitis was also considered as a possible diagnosis.

A CT scan of the chest, abdomen and pelvis identified no malignancy. A magnetic resonance imaging (MRI) scan of the spine to investigate for possible spinal cord compression was also normal.

The patient continued to complain of urinary frequency over the subsequent days and the ward nurses commented that his urine was exceptionally dark in colour. After 10 days of investigation, the patient's urine was sent for urinary porphyrins. The results showed very high levels of porphyrins and subsequent genetic testing confirmed a diagnosis of acute intermittent porphyria.

Final diagnosis: Acute intermittent porphyria.

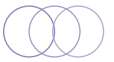
OUTCOME

The patient commenced treatment with heme arginate and made a good recovery over the subsequent fortnight. He returned to work but has subsequently had a further hospital admission with another episode of acute intermittent porphyria.

CASE DISCUSSION

Acute intermittent porphyria is an autosomal dominant metabolic disorder characterised by a deficiency in uroporphobilinogen deaminase. Patients with the condition tend to manifest symptoms of an acute attack in the presence of factors including drugs (such as certain calcium channel blockers, antifungal agents and anaesthetics) and dietary changes. There was no clear precipitant in this patient, although his anorexia will certainly have exacerbated the attack.

Abdominal pain is the most common presenting complaint, but patients may also exhibit features of peripheral neuropathy and proximal muscle weakness. Urinary symptoms, including both retention and incontinence, are common. In this case, the patient described noticing dark urine at the time of collapse, but this was not felt to be of relevance until later, as jaundice had been excluded and the discolouration was likely attributed to dehydration with concentrated urine.



Heme arginate, an inhibitor of aminolevulinic acid synthase, is used as the drug of choice to treat acute episodes. It acts to reduce the accumulation of δ -aminolevulinic acid that occurs in episodes of acute intermittent porphyria.

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CASE 38: A HYPERNATRAEMIC PATIENT

PATIENT HISTORY

An 82-year-old woman was brought to hospital after her husband called for an ambulance. He described a 2-week decline in his wife's mobility, which had progressed from her walking outdoors independently to now only walking a few steps indoors with his assistance. The patient's husband said that she had become confused and was not orientated to time or place. She had also developed new urinary incontinence over the preceding fortnight. The patient had been refusing food and water for the past 24 hours, which had prompted the telephone call to the emergency services. The patient had been diagnosed with Alzheimer's disease several years ago and had longstanding hypertension. She took 5 mg amlodipine OD but no other medications. She had worked as a judge until the age of 65 and had maintained an active lifestyle until recent months. No further history was available at this point. The ambulance crew described the patient's husband as also being confused, although significantly less so than his wife.

EXAMINATION

Initial observations: T 36.1°C, HR 88 bpm, BP 146/92 mm Hg, RR 14 and SpO₂ 98% on room air.

The patient was confused and withdrawn. She obeyed most commands and responded with 'yes' and 'no' responses to questions but otherwise engaged poorly. Her mucous membranes were dry and her jugular venous pressure (JVP) was not visualised. Cardiovascular examination was otherwise unremarkable. Respiratory and abdominal examinations identified no abnormalities. Neurological examination identified generalised weakness of the limbs (power 4/5 throughout), but the tone and reflexes were normal. Cranial nerve examination was unremarkable. The patient refused to walk so her gait was not observed. The patient was incontinent of urine during the examination. She had no point spinal tenderness. There was no saddle anaesthesia and anal tone was normal.

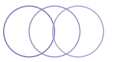
INITIAL RESULTS

Routine blood tests: WCC 19.5, N^o 18.1, L^o 1.2, Hb 141, MCV 92, Plt 191, Na 158, K 4.0, Urea 23.0, Creat 177 (no baseline available), liver function tests (LFTs) – all within reference range, CRP 422.

DIFFERENTIAL DIAGNOSES

In this patient with increased confusion, poor mobility, urinary incontinence and elevated inflammatory markers, a urinary tract infection is the most likely diagnosis. All infections, including community-acquired pneumonia, cellulitis and meningoencephalitis may also cause confusion resulting in urinary incontinence so a basic septic screen should be performed.

Normal pressure hydrocephalus (NPH) classically presents with the triad of cognitive decline, urinary incontinence and a broad-based gait. This patient has an acute-on-chronic confusional state with new urinary incontinence, as well as reduced mobility which may



be due to gait dysfunction. A computed tomography (CT) scan of the brain will need to be performed to look for dilated ventricles in keeping with NPH. The CT scan will also exclude a subdural haematoma which may have developed several weeks earlier, although there was no history of a recent fall or head injury. A space-occupying intracranial lesion, such as a malignancy, may also be seen.

Hypothyroidism and electrolyte disturbances, such as hypercalcaemia, should also be considered. The patient is hypernatraemic – this could be due to dehydration (i.e. hypovolaemia), as reflected by her impaired renal function, or may represent diabetes insipidus (DI).

HOW WOULD YOU MANAGE THE PATIENT ACUTELY?

A basic septic screen, including a chest x-ray and blood cultures (even in the absence of fever) should be performed. The patient is incontinent of urine so it may not be possible to obtain a urine sample. Some physicians recommend temporary insertion of a urinary catheter for the sole purposes of obtaining a sample. In this case we will need to site a urinary catheter to closely monitor the patient's fluid balance and will obtain an initial urine sample via this route. Paired urine and serum osmolalities and a urinary sodium level should be measured.

Broad-spectrum antibiotics should be commenced. An antibiotic that will provide good gram-negative cover should be prescribed in view of the possible urinary source of sepsis.

The patient is hypovolaemic and will require intravenous fluids. A good choice for the bag of fluids is 1 L of compound sodium lactate (Hartmann's solution), as this contains sodium (but less than 0.9% saline) and potassium and is less likely to precipitate rapid electrolyte shifts than 0.9% saline. If the plasma sodium level falls too quickly, the reduction in plasma osmolality may cause cerebral oedema to develop. The patient's fluid status should be reassessed every 2–4 hours initially and further decisions regarding fluid choice should be based on her urine output and her plasma sodium level. You should aim to allow serum sodium levels to fall by no more than 8–12 mmol in 24 hours, to prevent the development of central pontine myelinolysis.

A CT scan of the brain, to identify a space-occupying lesion or intracranial bleed should also be carried out.

CASE PROGRESSION

The patient was treated with intravenous co-amoxiclav for a presumed urinary tract infection. A urine sample was not obtained until after antibiotics had been given and subsequently showed no bacterial growth.

Repeat blood tests were performed 24 hours later. The serum sodium level had risen to 172 mmol/L. Her urine output was high, at around 250 mL/hr, and the medical team were struggling to match her fluid input and output. She was receiving intravenous 5% dextrose but remained in negative fluid balance. She was taken to the high dependency unit for closer monitoring of her intravascular volume and sodium level.

Her plasma osmolality remained at around 360 and a paired urinary osmolality was low. She remained withdrawn with low motivation to self-care. She drank no fluid without encouragement. A nasogastric tube was sited to aid nutrition and hydration. A provisional diagnosis of DI was made. The endocrinology team performed a desmopressin response test (see below) and established that the patient had probable nephrogenic DI.



Further history subsequently emerged following discussions from the patient's children who stated that their mother had a lifetime history of polydipsia, polyuria and nocturia. It was felt that the patient had probably developed DI during early adulthood but had remained well due to high water intake, replacing her fluid losses. As her dementia progressed, her thirst response was lost and she was not able to maintain adequate water intake, leading to the development of hypernatraemia.

Final diagnosis: Nephrogenic DI.

OUTCOME

Bendroflumethiazide (a thiazide diuretic) was commenced and the patient's fluid status gradually improved until she was euvolaemic with serum sodium levels at the upper limit of normal. Her cognitive function did not return to baseline and she was discharged to a nursing home for further care.

CASE DISCUSSION

There are four major causes of polyuria – diabetes mellitus, psychogenic polydipsia, cranial DI and nephrogenic DI. Diabetes mellitus is diagnosed following measurements of blood glucose and HbA1c while psychogenic polydipsia is diagnosed by monitoring sodium levels and osmolality following a water deprivation test.

In this case, DI was established as a probable diagnosis early into the admission. The team next attempted to establish whether this was cranial or nephrogenic DI. A magnetic resonance imaging (MRI) scan of the brain showed no mass lesions. Intravenous desmopressin (an anti-diuretic hormone [ADH] analogue) was administered and the urine osmolality and volume were measured closely over the next 2 hours. There was no demonstrable change in urine osmolality or volume following desmopressin administration. This indicated that her kidneys did not respond appropriately to desmopressin (nephrogenic DI) rather than impaired hypothalamic production of ADH (i.e. central DI) being present.

Cranial DI can be treated by regular administration of desmopressin in addition to a low-solute diet. Nephrogenic DI is typically managed with a combination of diuretics, non-steroidal anti-inflammatory drugs (NSAIDs) and a low-solute diet.

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CASE 39: A YOUNG PATIENT WITH A CHRONIC COUGH

PATIENT HISTORY

A 47-year-old woman presented to the rheumatology outpatient clinic complaining of a chronic, non-productive cough. She described 2–3 months of progressive coughing and shortness of breath on exertion. She had experienced low-grade fevers over recent weeks but was still managing to attend her job where she worked as a supermarket cashier. She denied both night sweats and weight loss. She had a past medical history of rheumatoid arthritis for which she took oral methotrexate. She also took regular folic acid treatment. She lived with her sister, did not smoke tobacco or cannabis and drank around 10 units of alcohol weekly. She had not travelled abroad in the preceding 1 year and had no recent unprotected sexual intercourse.

EXAMINATION

Initial observations: T 37.5°C, HR 84 bpm, BP 116/72 mm Hg, RR 14 and SpO₂ 91% on arrival to clinic, 97% when repeated after 5 minutes of rest.

The patient appeared comfortable at rest. There were bilateral coarse crackles at the middle and lower zones of her lungs. Cardiovascular and abdominal examinations were unremarkable. Neurological examination was not performed. Of note, there were no rashes and the patient had no palpable lymphadenopathy.

INITIAL RESULTS

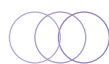
Routine blood results: WCC 15.5, N^o 12.1, L^o 2.9, Hb 152, Plt 223, Na 140, K 3.7, Creat 80 (no baseline available), CRP 101.

DIFFERENTIAL DIAGNOSES

The patient has a low-grade fever, cough and her oxygen saturations fall significantly upon exercise, despite looking relatively well. Her blood results show elevated inflammatory markers. The patient almost certainly has community-acquired pneumonia. This is commonly due to a bacterial or viral infection, but in this case, where the patient is immunosuppressed with methotrexate, a fungal infection could also be possible, particularly *Pneumocystis jirovecii*. Hypoxia that exceeds expectations based on the patient's symptoms is a typical feature of *Pneumocystis jirovecii* pneumonia (PCP).

Another possibility would be a pulmonary *Mycobacterium tuberculosis* infection, particularly in view of the fact that the patient is immunosuppressed.

Malignancy should be considered, such as a primary lung cancer, or secondary lung metastasis with, for example, a primary bowel or breast malignancy.



HOW WOULD YOU MANAGE THE PATIENT ACUTELY?

Broad-spectrum antibiotics to cover for a possible bacterial pneumonia should be commenced. The patient should be admitted to hospital for further investigations. She will require a chest x-ray to identify signs of infection or abnormal mass lesions. In terms of investigations for pulmonary tuberculosis, sputum samples should be sent for acid-fast bacilli (AFB) analysis. Blood cultures and early morning urine samples may also be sent for AFB analysis if appropriate.

Sputum must be sent for bacterial culture and the microbiologist should also be asked to test the sample for *Pneumocystis jirovecii*. If the patient is unable to expectorate sputum, an induced sputum sample may be obtained with the use of nebulised hypertonic saline. A viral nasal/throat swab should also be taken to screen for respiratory viruses, including rhinovirus and influenza A.

If pulmonary tuberculosis is strongly suspected and the patient is producing sputum, the patient will need to be managed in an isolated negative-pressure room to prevent disease spread.

CASE PROGRESSION

The patient was admitted to hospital and commenced on broad-spectrum intravenous antibiotics. A chest x-ray was performed (see [Figure 39.1](#)), showing bilateral perihilar infiltrates, in keeping with PCP. She was unable to provide a sputum sample and therefore required nebulised hypertonic saline and chest physiotherapy to induce sputum expectoration.

Sputum samples showed no AFBs, but sputum cultures grew *Pneumocystis jirovecii*. The patient commenced co-trimoxazole (combined trimethoprim and sulfamethoxazole) therapy and initially made a good recovery, but several days after commencing treatment, she developed worsening shortness of breath and appeared cyanotic. An arterial blood gas showed hypoxia with a picture of type 1 respiratory failure. The blood sample was initially thought to be venous in origin due to a brownish discolouration. The methaemoglobin level was noted to be elevated at 16% (reference range <1%). Methaemoglobinaemia is a known side effect of both co-trimoxazole, and the second-line agent for PCP treatment, dapsone. The patient was treated with supplemental oxygen therapy targeting an SpO₂ range of 94%–98% and received intravenous methylene blue 1% solution, which is an antidote capable of reducing methaemoglobin to haemoglobin.

Final diagnosis: *Pneumocystis jirovecii* pneumonia (PCP).

OUTCOME

The patient's PCP was subsequently treated with atovaquone and she made a good recovery over the following weeks.

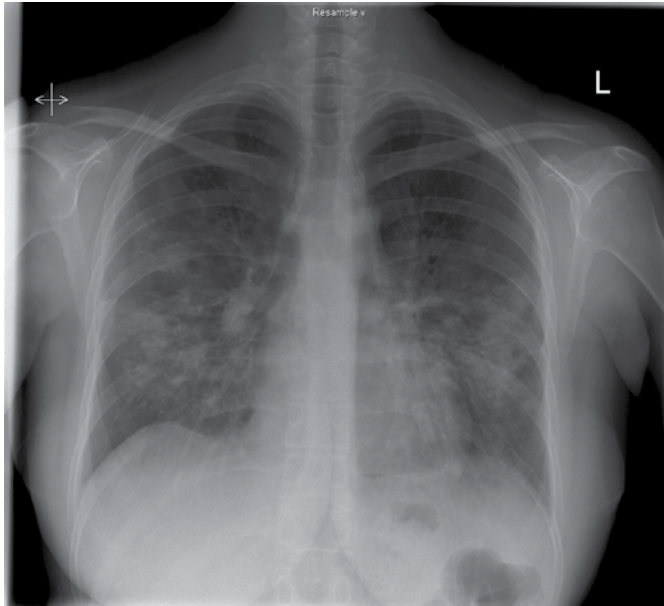
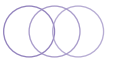


Figure 39.1 Chest x-ray showing bilateral perihilar infiltrates.

CASE DISCUSSION

PCP is a fungal infection that is present in many healthy individuals but primarily affects immunocompromised people. Rather than presenting acutely, the infection typically develops over a time course of weeks to months and early chest x-rays may even appear normal.

Fungal spores infiltrate the lung tissue, leading to a progressive pneumonia, which is often bilateral. Patients may be hypoxic, particularly after exertion, despite looking relatively comfortable. Additional symptoms such as weight loss, fevers and night sweats may be present.

Upon confirmation of the diagnosis, patients will begin treatment with anti-pneumocystic medication, such as co-trimoxazole or dapsone. Corticosteroids are also given to reduce pulmonary inflammation in moderate–severe cases.

Patients who are at high risk of developing PCP, such as those receiving chemotherapy, people taking immunosuppressant medication, or patients with HIV infection and low CD4 counts (<200 cells mm^3), are often commenced on prophylactic anti-pneumocystic medication to prevent development of the condition.

Pneumothorax is a relatively common presenting feature of PCP infection, due to the formation of subpleural necrosis and pleural blebs, which make the tissue prone to rupturing. Bilateral pneumothoraces may develop in severe cases.

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CASE 40: RECURRENT ABDOMINAL PAIN AND DIARRHOEA

PATIENT HISTORY

A 42-year-old man presented to the emergency department complaining of recurrent episodes of abdominal pain. He had attended the emergency department twice previously over the past 2 months, complaining of abdominal pain that had resolved with simple analgesia on each occasion. The pain was dull and cramping in nature and came on intermittently three to four times daily, lasting for approximately 20 minutes. The pain was relieved by opening his bowels. The patient also complained of 4 months of passing loose stools mixed with mucus, but denied any rectal bleeding or melaena. He had not vomited and had maintained a normal appetite. The patient had no past medical history and took no regular medications, although he had been occasionally using loperamide to relieve his diarrhoea over recent weeks. He was an ex-smoker with a 3 pack year smoking history. He drank around 8–10 units of alcohol per week. He worked as a train guard and lived with his wife and daughter. His last travel abroad was to Geneva 1 year ago. He denied feeling feverish or losing weight, but the patient's wife reported that he appeared flushed in the evenings.

EXAMINATION

Initial observations: T 36.9°C, HR 88 bpm, BP 140/74 mm Hg, RR 14, SpO₂ 100% on room air.

The patient appeared well and was comfortable at rest. His chest was clear to auscultation. His heart sounds were normal and there were no signs of cardiac disease. His abdomen was soft but generally tender, particularly over the umbilical region, where there was some voluntary guarding on deep palpation. Bowel sounds were normal. Neurological examination was not performed.

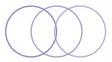
INITIAL RESULTS

Routine blood results: WCC 9.4, Hb 148, MCV 80, Plt 179, Na 132, K 3.6, Creat 100 (baseline 80 2 years ago), CRP 3, Amylase 47 (checked 1 week earlier, unchanged), Bili 40, ALT 59, ALP 78, Alb 39.

DIFFERENTIAL DIAGNOSES

The patient complains of recurrent episodes of abdominal pain associated with diarrhoea. Blood tests show no elevation in inflammatory markers, while hyponatraemia and impaired renal function have developed, likely secondary to diarrhoea.

Inflammatory bowel disease, such as Crohn's disease or ulcerative colitis, is a possible diagnosis, although a rise in inflammatory markers would typically be observed. The patient should, nevertheless, be investigated for this.



Gastroenteritis is another possibility although, again, one would expect an elevation in inflammatory markers to be present. The duration of illness is longer than would be expected for simple gastroenteritis, although recurrent infections can occur, particularly if the patient has underlying immunosuppression, such as HIV infection. Infections, such as *Clostridium difficile* may present with chronic diarrhoea. Pancreatitis is also unlikely, given the normal amylase level on repeated measures.

Coeliac disease should also be considered. This autoimmune disease can present with a variety of symptoms affecting all systems but may develop simply with diarrhoea and abdominal pain. Tropical sprue would be a possible cause of the symptoms if the patient gave a more extensive travel history.

Hyperthyroidism can present with diarrhoea and abdominal pain, although other features such as palpitations are generally present.

Last, cancer, such as small bowel lymphoma, should be considered. The examination has not identified whether lymphadenopathy is present. Although malignancy may not seem particularly likely, it is important to exclude due to the potentially serious consequences.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

Now that the patient has re-presented, his abdominal pain warrants further investigation, although not necessarily in the inpatient setting. A plain abdominal x-ray should be performed to look for signs of bowel obstruction. Liver function tests and a coagulation test (INR) should be checked to identify potential hepatic dysfunction. The patient is able to eat and drink and does not need intravenous fluids at present, but his renal function and sodium level should be re-checked to ensure there is no deterioration.

Serological tests to identify coeliac disease, such as anti-transglutaminase antibodies, anti-endomysial antibodies and total serum IgA levels should be sent. An HIV test should also be taken. If malabsorption is suspected, it would be prudent to check vitamin B₁₂, folate and iron levels as these may need to be corrected.

Stool samples should be sent for microscopy, culture and sensitivities (MC&S) to identify potential pathogens, as well as for a faecal calprotectin level, which is a marker of intestinal inflammation that is elevated in the presence of inflammatory bowel disease. An abdominal ultrasound scan should be requested to look for any mass lesions that could represent malignancy or other pathologies such as gallstones.

The case should be discussed with the gastroenterology team who may wish to investigate further with a sigmoidoscopy or colonoscopy, to identify potential inflammatory bowel disease. There is no indication for an oesophago-gastro-duodenoscopy (OGD) at present, although this may be considered depending on the results of the lower gastrointestinal endoscopy.

CASE PROGRESSION

An abdominal x-ray was unremarkable. The patient continued to have pain and diarrhoea over the next 24 hours and remained under inpatient care. Simple analgesia partially relieved the pain and stronger analgesia was declined. Stool samples were sent but yielded no abnormal findings.



An abdominal ultrasound scan showed two irregular lesions within the liver that appeared to be metastatic lesions. A computed tomography (CT) scan of the abdomen and pelvis subsequently identified multiple metastatic deposits within the liver and mesentery with a large ileal mass. An ileal biopsy was performed and this showed tissue consistent with a primary carcinoid tumour.

A 24-hour urinary collection was sent for 5-HIAA (a metabolite of serotonin) levels, which were significantly elevated, consistent with a diagnosis of carcinoid syndrome.

Final diagnosis: Neuroendocrine tumour with carcinoid syndrome.

OUTCOME

The patient underwent a partial resection of his primary tumour to prevent the development of intestinal obstruction. He has responded well to octreotide therapy and is maintaining an independent life at home. He is aware that his disease is likely to progress over the coming months.

CASE DISCUSSION

Carcinoid tumours typically arise from the gastrointestinal tract, particularly within the appendix. Tumours that develop outside the appendix are frequently malignant. Carcinoid tumours are neuroendocrine in origin and produce serotonin, gastrin and adrenocorticotrophic hormone (ACTH).

The classical symptoms of diarrhoea, flushing and wheeze, which comprise carcinoid syndrome, develop as a result of excessive production of serotonin (which is converted to 5-HIAA). Carcinoid syndrome occurs in around 5% of patients with carcinoid tumours and only develops once hepatic metastases are present, as the liver will otherwise metabolise serotonin within the gastrointestinal tract.

In some cases, excessive serotonin levels can lead to fibrosis of the tricuspid and pulmonary valves. In this case, the patient was found to have moderate tricuspid regurgitation when a transthoracic echocardiogram was performed and he is now being considered for cardiac valve surgery.

Carcinoid syndrome is treated with octreotide, an analogue of somatostatin, which suppresses the release of certain gastrointestinal hormones and increases intestinal transit time to relieve symptoms of diarrhoea.

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CASE 41: SEIZURES AND HAND LESIONS

PATIENT HISTORY

A 52-year-old man was admitted to hospital after having a tonic-clonic seizure in the street. The seizure lasted for 4–5 minutes and self-terminated. A community support police officer who witnessed the event said that the patient was well-known to him and described episodes where he had consumed excessive quantities of alcohol and was subsequently found in a confused and aggressive state. The patient was of no fixed abode. The patient was drowsy and no further history was available at this point.

EXAMINATION

Initial observations: T 35.8°C, HR 78 bpm, BP 146/90 mm Hg, RR 12, SpO₂ 97% on room air.

The patient was drowsy with a Glasgow Coma Scale (GCS) score of 10 (eyes – 2, verbal – 3, movement – 5), but this was gradually improving. His pupils were size 4 (normal) bilaterally and reacted to light. Tone was normal throughout all limbs and reflexes were present and symmetrical. Power could not be assessed, but the patient was moving all four limbs. He appeared to have an enlarged tongue and there were signs that he had bitten both his tongue and his lips during the seizure. His hands (see [Figure 41.1](#)) were noted to have multiple excoriated lesions over the fingers with patches of exudate on the dorsal aspects and desquamation over the plantar aspects. There were no track marks over antecubital fossae, indicative of intravenous drug use. His chest was clear to auscultation and his heart sounds were normal. His abdomen was soft and non-tender. No lymphadenopathy was identified.

INITIAL RESULTS

Routine blood tests: WCC 80, N° 6.2, L° 1.4, Hb 110, MCV 108, Plt 298, Na 135, K 4.8, Creat 57, CRP 4.

DIFFERENTIAL DIAGNOSES

This patient is known to drink alcohol to excess and has a history of being found in a confused and aggressive state. Without further information, chronic alcoholism with an alcohol withdrawal seizure is currently the most likely diagnosis. Alternatively, he may have a past medical history of epilepsy and the possible seizure could be secondary to this. The fact that his consciousness level is improving is suggestive of a post-ictal state and the tongue biting is in keeping with a seizure.

Korsakoff's dementia is a neurological disorder caused by thiamine deficiency that occurs frequently in patients with alcohol dependency. Patients present with amnesia and confabulation. Wernicke's encephalopathy also develops secondary to thiamine deficiency and presents with ataxia, confusion and, in some cases, ophthalmoplegia. The patient may have a background of Wernicke–Korsakoff syndrome and should be treated for this.

An intracranial pathology, such as a subdural haematoma, should also be considered. Patients with a history of chronic alcohol abuse are at a higher risk of both cerebral atrophy and



Figure 41.1 Lesions over the patient's fingers.

traumatic head injury, often with an underlying clotting impairment, and this diagnosis can be easily overlooked while symptoms of reduced consciousness are attributed to intoxication.

Other cerebral space-occupying lesions, including malignancy or infections, such as cerebral tuberculosis or toxoplasmosis are a possible cause of seizures and drowsiness, particularly if there is any underlying cause for immunosuppression.

Meningoencephalitis should be considered in any patient with an acutely altered level of consciousness. The fact that the patient is afebrile with no fever, nuchal rigidity or increase in inflammatory markers makes this less likely.

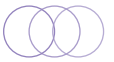
With respect to the lesions in the patient's fingers, they appear to represent a bacterial infection, such as impetigo, with generalised oedema and erythema of the surrounding skin. This could signify underlying immunosuppression.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

In view of the patient's history of alcohol misuse, he should be closely monitored for signs of alcohol withdrawal, such as tremors or sweating. If there are signs of withdrawal, benzodiazepines, such as chlordiazepoxide, should be commenced to limit symptoms and reduce the risk of withdrawal seizures.

To prevent (or possibly, in this instance, to treat) Wernicke–Korsakoff syndrome, a high-potency vitamin infusion containing thiamine, riboflavin, pyridoxine, niacin and ascorbic acid should be given.

A computed tomography (CT) head scan should be performed to exclude a subdural or intracranial bleed, and to look for a space-occupying lesion, such as a tumour, which may have precipitated a seizure or reduced level of consciousness.



The patient's consciousness level should be monitored, with neurological observations being performed at least hourly initially, to identify any deterioration in consciousness. If there is ongoing concern about potential meningoencephalitis, an intravenous antibiotic (e.g. cefuroxime) and antiviral agent (e.g. aciclovir) should be considered.

CASE PROGRESSION

The patient's consciousness level improved over the next 30–60 minutes and his initial drowsiness was attributed to a post-ictal state. The patient was aggressive and disorientated over the subsequent days, despite effective treatment for potential alcohol withdrawal.

The dermatology team reviewed the lesions on the patient's hands and diagnosed a bacterial skin infection with areas of underlying dermatitis. They also noticed patches of alopecia over the scalp and the presence of glossitis. The patient was unable to recall his personal details or home address. He spoke with a strong Welsh accent and was unsure if he had lived in England for a number of years or whether he had travelled here more recently. He had significant short-term memory impairment and was unable to retain information between conversations, frequently finding himself disorientated on the ward. The police were notified and they planned to search their missing person records.

The neuropsychiatry team assessed the patient and felt that signs of confusion, aggression, dermatitis and glossitis were in keeping with a diagnosis of pellagra. Blood tryptophan levels were sent, which confirmed the diagnosis.

Final diagnosis: Pellagra.

OUTCOME

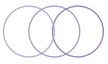
Following nicotinamide (a niacin amide) replacement therapy, the patient gradually improved. He was able to recall his name and year of birth and his family were eventually traced. He had been reported missing from his home approximately 150 miles away 6 months earlier. He returned home to complete his rehabilitation and was eventually able to manage an independent life, although he has continued to misuse alcohol and has frequent falls.

CASE DISCUSSION

Pellagra is a multisystem disease, which develops in the presence of niacin (B vitamin) deficiency, typically affecting patients with malabsorption or poor nutritional intake. Patients with chronic alcohol misuse may be at risk of developing this condition.

Symptoms include confusion and aggression, progressing to dementia, and signs of dermatitis, as well as chronic diarrhoea may also be present. Some patients may additionally develop glossitis or laryngitis.

Diagnosis is confirmed following demonstration of rapid resolution of symptoms following high-level nicotinamide replacement therapy, but low serum niacin and tryptophan levels may support the diagnosis.



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CASE 42: BILATERAL FOOT WEAKNESS

PATIENT HISTORY

A 47-year-old man presented to hospital complaining of worsening bilateral foot pain and weakness that was worse when he walked or ran. The symptoms had developed over the preceding 2 days, with pain initially present in the arches of his feet only. The pain progressed to involve his heels over the next 24 hours and was described as an intense, burning pain. His calves had been tender to touch on the morning of presentation. He complained of feeling as though his legs may give way when walking, but suspected that the weakness may be secondary to pain. He denied recent trauma to the lower limbs. He took spinning classes once weekly and had initially attributed his symptoms to post-exercise myalgia. He denied recent immobility or long-haul travel, and had no previous or family history of venous thromboembolism. His past medical history included asthma and a diagnosis of cleft palate at birth, which had been corrected in infancy. He took no regular medications. The patient worked as an office manager and lived alone. He denied ever smoking and usually drank 15–20 units of alcohol per week. He denied recent unprotected sexual intercourse. He travelled to Austria three times per year to visit family.

EXAMINATION

Initial observations: T 36.9°C, HR 96 bpm, BP 140/80 mm Hg, RR 20, SpO₂ 98% on air.

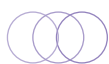
The patient walked through the emergency department to be examined in a cubicle and was noted to have an antalgic gait, leaning on a member of staff to minimise weight bearing on his lower limbs. Respiratory, cardiovascular and abdominal examinations were unremarkable. Neurological examination identified reduced sensation to pin prick in all toes. The feet and calves were noted to be tender on palpation with no sensory impairment. Examination of power in the lower limbs was somewhat limited by pain and was found to be 4+/5 throughout. Of note, however, hip flexion and extension were both graded at 4+/5 despite no pain being present in these regions. Upper limb examination was unremarkable and the cranial nerves were intact. No joint swelling or rashes were present.

INITIAL RESULTS

Routine blood tests: WCC 10.2, N^o 8.0, L^o 2.0, Hb 153, Plt 340, Na 140, K 4.2, Creat 62, CRP 24.

DIFFERENTIAL DIAGNOSES

The patient describes pain of the feet and calves with weakness in the same regions, which he attributes to pain. He does, however, have objective weakness in the hips despite having no pain in this area. The differential for localised myalgia includes muscle overuse, which may be applicable in this case as the patient reports an intense exercise regime. Rhabdomyolysis can develop following extreme muscle strain and renal function and creatine kinase levels should therefore be monitored.



Compartment syndrome and muscle infarction would be suspected in unilateral localised myalgia, but these conditions would be very unlikely to develop bilaterally. Pyomyositis would also be expected to develop unilaterally and there is typically a history of a fever.

An inflammatory myopathy, such as polymyositis, can be idiopathic or associated with malignancy, and typically affects proximal rather than distal muscle groups. Certain medications, particularly statins, may lead to a widespread myalgia.

Systemic infection with bacterial organisms, or viral infections, for example influenza, may present with myalgia. The patient has a mild neutrophilia and elevated C-reactive protein (CRP) level, which could indicate that an infection is present. *Borrelia* infection (Lyme disease) following tick bites may present with muscular and joint pain, although typically over a longer time course. Tick-borne Lyme disease is prevalent throughout the Northern hemisphere.

This could represent a first presentation of type 2 diabetes mellitus, with diabetic neuropathy causing pain. The burning nature of the pain and the apparent stocking distribution point toward a symmetrical polyneuropathy – excessive alcohol consumption, vitamin B deficiencies and HIV are potential causes.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

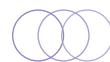
Serum creatine kinase levels should be sent to assess for an abnormally high level of muscle breakdown. An HIV test should be performed. A blood glucose and a HbA1c level should be taken. Thyroid function, vitamin B₁₂ and folate levels should also be measured, in addition to an autoimmune screen.

Formal neurophysiology investigations, such as nerve conduction testing, may be considered, as well as a nerve biopsy, but these could potentially be performed in the outpatient setting, depending on how the patient progresses. Further management options will be determined by the final diagnosis.

CASE PROGRESSION

Over the subsequent 48 hours, the patient developed rapidly progressive weakness of the upper limbs, initially in a symmetrical distribution but eventually extending to involve the left upper arm only. The pain in the lower limbs resolved but the weakness progressed, with proximal power falling to 3/5 and distal power reaching 4-/5. No facial weakness developed. Deep tendon reflexes were diminished on repeat neurological examination.

Following nerve conduction studies, which showed areas of demyelination and the change in clinical picture, a diagnosis of acute inflammatory demyelinating polyradiculoneuropathy (AIDP; formally known as Guillain-Barre syndrome) was made. Bedside spirometry was conducted four times daily to monitor the patient's forced vital capacity, as the respiratory muscles may be involved in severe cases of AIDP, leading to impaired respiratory function and possible respiratory arrest. The patient's respiratory function was initially normal but deteriorated over a period of 36 hours. He was transferred to the high dependency unit where his respiratory function could be closely monitored and intubation could be performed pre-emptively if required.



A course of intravenous immunoglobulin (IVIg) was commenced and over the next 2 weeks, the patient gradually improved. Plasmapheresis was considered but was deemed unnecessary following a good response to IVIg therapy. Mechanical ventilation was not required at any stage.

Final diagnosis: Acute inflammatory demyelinating polyneuropathy.

OUTCOME

The patient required several months of rehabilitation before he was able to return to work. Stool samples and serology were sent specifically to identify a possible antecedent *Campylobacter* infection, which is a common trigger for AIDP. There was serological evidence of a recent *Campylobacter jejuni* infection, but the patient denied symptoms of diarrhoea prior to his presentation.

CASE DISCUSSION

This case was particularly challenging as the patient initially presented with pain rather than the classical AIDP features of progressive, ascending weakness with areflexia. AIDP is an autoimmune process that often develops following an antecedent infection with *Campylobacter jejuni* or a viral infection such as influenza, HIV, Epstein–Barr or cytomegalovirus. Respiratory muscle involvement may rapidly progress to respiratory failure requiring intubation and mechanical ventilation. The condition is treated with immunotherapy, consisting of either plasmapheresis or IVIg infusion. Although pain is not a common presenting feature (indeed, impaired sensation is frequently reported), in some cases, intense neuropathic pain may accompany the development of peripheral weakness.

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CASE 43: RASH, FEVERS AND HEADACHE

PATIENT HISTORY

A 23-year-old medical student returned from his 8-week elective placement in India and attended hospital within hours of returning to the United Kingdom. He complained of a 2-day history of high fevers, nausea and headaches. He had vomited twice that day and also described a vivid maculopapular rash over his trunk, which had faded over the duration of his flight home. His friends who had accompanied him for his hospital placement had examined him prior to their flight home and had identified both neck stiffness and photophobia. The patient described widespread myalgia and arthralgia but denied joint swelling. He had no significant past medical history and took no regular medications. He admitted to occasional amphetamine use but had never injected drugs. He had unprotected sexual intercourse with a female partner several times during his recent trip to India. He had not travelled elsewhere during the preceding 12 months. He had not taken malaria prophylaxis or used insect repellent. His travelling companions were well.

EXAMINATION

Initial observations: T 38.2°C, HR 102 bpm, BP 120/66 mm Hg, RR 14, SpO₂ 100% on room air.

The patient looked well and was comfortable at rest. Respiratory, cardiovascular and abdominal assessments were unremarkable. There was no neck stiffness, no photophobia and Kernig's sign was not present. Cranial nerve and limb examinations were normal. There was no palpable lymphadenopathy. No rash was observed, but there were multiple insect bites on the patient's ankles.

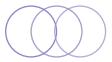
INITIAL RESULTS

Routine blood tests: WCC 21.7, N° 14.0, L° 5.9, Hb 152, Plt 297, Na 137, K 3.7, Creat 71, CRP 80, Bili 14, ALT 18, ALP 20, INR 1.1.

DIFFERENTIAL DIAGNOSES

For this case you need to consider the vast topic of fever in a returning traveller. The patient has been travelling in India where malaria is present and he has visible insect (possibly mosquito) bites on his ankles. The patient has a normal haemoglobin level and platelet count, and his renal function is not impaired, all of which may become deranged with severe malaria infection, particularly with *Plasmodium falciparum* cases though *P. vivax* is also common in this part of the world. Typical features of malaria infection include fevers, headache, myalgia, diarrhoea and vomiting. Patients may develop jaundice, haemolytic anaemia and thrombocytopenia, and severe cases may have renal failure.

Dengue and chikungunya viruses are also transmitted via mosquito bites and can present with features similar to malaria, with headache, fever and arthralgia. Severe pain, described as 'breakbone pain' is a common feature of dengue fever. Chikungunya infection often



presents similarly to dengue fever, although bone pain is a less prominent feature, and it can be difficult to distinguish between the two conditions. Co-infection may also occur, as both pathogens are transmitted by the *Aedes aegypti* mosquito.

HIV seroconversion is another possibility, particularly as the patient admits to recent episodes of unprotected sexual intercourse. Rash, fever and flu-like symptoms are common features of a seroconversion illness. Viral (including Japanese encephalitis) or bacterial meningitis, syphilis, chlamydia and gonorrhoea should also be considered, in view of the history of fever and headache and unprotected sexual intercourse.

S. typhi and *S. paratyphi* are common in the Indian subcontinent and may present with fever and headache. *Brucella* can present in a similar way to typhoid fever.

Lastly, influenza is a common cause of all of the symptoms that the patient has complained of. When assessing a febrile returning traveller, it is important to remember that they are still at a far greater risk of developing infections and other pathologies aside from tropical diseases.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient is febrile and a full septic screen, including three sets of blood cultures (to improve the yield of detection of *S. typhi* and *paratyphi*), urine and sputum cultures, and a chest x-ray should be performed. In this case, three blood films should be taken, to identify possible malaria parasites. The on-call haematology technician or haematologist should be notified when the blood samples can be processed. The microbiology lab should be informed of the risk of typhoid or brucella so they can process the blood culture samples safely. Respiratory nasal swabs should be taken to identify potential influenza infection. Serum samples may identify the presence of dengue or chikungunya viruses and must be sent for testing for HIV and syphilis – the case should be discussed with the infectious diseases team to ensure testing accounts for current pathogens in that location (e.g. Zika virus).

A blood gas sample (arterial or venous) should be taken to assess for the presence of a metabolic acidosis and/or a lactataemia, which will allow you to assess the patient's clinical condition more accurately. The patient is tachycardic and febrile and therefore intravenous fluid therapy should be commenced, along with assessment of his urine output and fluid balance status.

Although there may not be a clear diagnosis at this stage, the possibility of meningitis means that broad-spectrum antibiotics suitable for cerebrospinal fluid (CSF) penetration should be commenced. More focused therapy can be substituted once further information, such as blood culture results, is available. A lumbar puncture should be performed.

CASE PROGRESSION

The patient was seen by the medical team who felt that the most likely diagnosis was viral meningitis. A lumbar puncture was performed prior to the administration of antibiotics and aciclovir. The initial CSF report showed no white or red cells present, as well as a negative Gram stain and a normal protein count. Three consecutive malaria films (taken 6 hours apart) were negative. Blood cultures did not reveal typhoid or brucellosis and chlamydia and gonorrhoea testing was negative. CSF was sent to a reference laboratory to exclude Japanese encephalitis.



The patient made a good recovery over the next 24 hours and his fevers settled. He was discharged the following day with no clear diagnosis for his symptoms. He was followed up 2 weeks later in the infectious diseases clinic where serology samples were found to be positive for chikungunya virus.

Final diagnosis: Chikungunya virus.

OUTCOME

The patient remained well and was able to educate his junior doctor colleagues about chikungunya infection the following year, when a patient was admitted under his care with the condition.

CASE DISCUSSION

In this case, a mosquito-borne virus, such as malaria, dengue fever or chikungunya virus was suspected. Chikungunya virus is an arbovirus that is transmitted by the *Aedes aegypti* mosquito. Symptoms are similar to dengue fever and include pyrexia, headache, a maculopapular rash (which this patient had prior to his presentation) and polyarthrititis. The disease is self-limiting and there is no specific treatment, although supportive therapy with intravenous fluids is sometimes necessary. Unlike dengue fever, haemorrhagic features are uncommon. Meningoencephalitis or acute flaccid paralysis can develop in severe cases.

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CASE 44: AN ELDERLY WOMAN WITH PAINLESS JAUNDICE

PATIENT HISTORY

An 89-year-old woman was referred to hospital by her general practitioner (GP) with jaundice. She was unclear when the jaundice had initially developed, but her son had first noticed it 2 weeks earlier and reported that the jaundice was progressing. Around 1 month earlier, she had been admitted to hospital with progressive shortness of breath and had been investigated for a presumed community-acquired pneumonia. A chest x-ray showed atelectasis at the right base plus a deviated trachea. A computed tomography (CT) scan of the chest, abdomen and pelvis (to investigate for possible malignancy) identified fibrotic changes at the right lung base but no other abnormalities. During the admission, the patient was noted to have developed deranged liver function with a marked transaminitis (bilirubin 8 $\mu\text{mol/L}$, ALT 245 IU/L, ALP 60 IU/L), which was attributed to a recent course of co-amoxiclav. She was discharged home after 2 days with a plan for her GP to review her in the community. Since then, the patient had remained dyspnoeic. She denied a cough or fever and there was no postural component to her dyspnoea. She complained of weight loss, although she was unable to quantify this further, as well as generalised lethargy and malaise. She denied pruritus and had no abdominal pain or change in bowel habit. Her stools were described as brown in colour, but she thought that her urine may be darker than it usually was. Her past medical history included hypertension, hypercholesterolaemia and recurrent urinary tract infections. She took regular 2.5 mg ramipril OD, 30 mg lansoprazole OD and 25 mg atenolol OD. She lived alone and had never smoked. She did not regularly drink alcohol and she had not travelled abroad in the preceding year. She was a retired script-writer who lived alone at home without assistance.

EXAMINATION

Initial observations: T 37.1°C, HR 62 bpm, BP 124/86 mm Hg, RR 17, SpO₂ 94% on room air.

The patient was obviously icteric, but there were no other stigmata of chronic liver disease. She appeared comfortable at rest. There were fine crackles at the right lung base, which the emergency department junior doctor described as 'velcro-like'. The heart sounds were normal and there was no peripheral oedema. Her abdomen was soft and non-tender with no palpable organomegaly.

INITIAL INVESTIGATIONS

Routine blood tests: WCC 7.2, Hb 10.7, MCV 80, Plt 250, Na 137, K 4.1, Creat 84 (baseline 80), CRP 6, Bili 178, ALT 1194, ALP 262, Alb 29, INR 1.1, cCa 2.75, Amylase 42.

DIFFERENTIAL DIAGNOSES

The working diagnosis from the patient's initial admission was that she had drug-induced hepatitis secondary to recent co-amoxiclav use. The combination of amoxicillin and

clavulanic acid that forms co-amoxiclav, is one of the most common causes of drug-induced hepatotoxicity in Europe, occurring in around 1 in 2500 instances. The onset of acute liver impairment is over days to weeks and patients typically present with a cholestatic picture, rather than an overt transaminitis. In some cases, patients may develop a hepatocellular pattern with an elevated alanine aminotransferase (ALT) or a mixed picture. Other drug causes of hepatitis should be considered and a detailed medication history should be taken from the GP if possible covering previous medications over the last 6 months. For example, amiodarone, a Class III anti-arrhythmic agent, can cause both pulmonary fibrosis and hepatitis.

Viral causes of hepatitis, such as hepatitis A, B, C or D, plus cytomegalovirus (CMV), Epstein-Barr virus (EBV) and HIV should be considered and serology can be sent to identify these.

In view of the history of weight loss and lethargy, an underlying malignancy may have developed, such as a primary hepatobiliary cancer (e.g. cholangiocarcinoma) or a malignancy with secondary liver deposits. The patient has a high corrected calcium level, which may have developed due to osteolytic metastases.

Autoimmune disease, such as primary biliary cirrhosis, is also a possibility. Non-alcoholic steatohepatitis or gallstone disease are other appropriate differential diagnoses. Hepatic vein thrombosis (Budd–Chiari syndrome) usually presents with abdominal pain with progressive ascites, neither of which are present in this case.

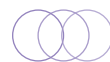
HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient appears to be relatively stable despite her deteriorating liver function. An urgent liver screen should be arranged, including serology for hepatitis viruses, CMV, EBV and HIV. Alpha-fetoprotein, a hepatocellular carcinoma and germ cell tumour marker, should also be measured. Given the patient's age, it would not be appropriate to send a serum caeruloplasmin level to be tested – symptoms of Wilson's disease usually present in childhood or early adulthood. An autoantibody screen (anti-mitochondrial antibody, anti-smooth muscle antibody and anti-nuclear antibody) will also need to be sent.

An abdominal ultrasound scan should be the initial modality of imaging. Depending on what this shows, other imaging studies may be needed. The patient had a CT scan of her chest, abdomen and pelvis only 1 month earlier, which did not identify a cause for her deranged liver function. It may be worth obtaining these images and reviewing them in the context of deteriorating liver function to identify a possible cause that was not seen on initial inspection.

The patient will undoubtedly have regular monitoring of her liver function enzymes, but it is important to check her INR (international normalised ratio, representing prothrombin time) as a measure of the liver's synthetic function of clotting factors. An elevated INR indicates that the patient has an increased risk of bleeding.

Some hospitals can measure the conjugated bilirubin component of the total bilirubin. If more than 50% is conjugated, this suggests conjugated hyperbilirubinaemia, which develops when the liver loses its excretory capacity. This is the case in the majority of liver diseases and cholestatic drug reactions. Unconjugated hyperbilirubinaemia may develop due to increased bilirubin production or reduced hepatic conjugation. Causes include Gilbert's syndrome and haemolysis.



CASE PROGRESSION

The patient remained stable overnight and an abdominal ultrasound scan was performed. This showed no obvious pathology. The following day, the patient's blood results showed worsening liver function, with an ALT level of 1450 IU/L. The radiology and gastroenterology teams advised a magnetic resonance cholangiopancreatography (MRCP) scan to visualise the biliary and pancreatic ducts. This showed very mild biliary duct dilatation but no focal cause for the patient's deranged liver enzymes. A triple-phase CT scan (using contrast to evaluate the early arterial, late arterial, and portal venous phases) was being considered to assess for the presence of hypervascular lesions that are otherwise challenging to identify, such as hepatocellular carcinoma.

At this point, a gastroenterology doctor took a focussed history and directly asked the patient about specific medications. He found that the patient had been taking the antibiotic, nitrofurantoin, for the preceding 6 months, until her current admission, to treat recurrent urinary tract infections. The patient had not disclosed this in her drug history as she did not think it was relevant. The team established that this was the most probable cause of her acute liver injury.

Final diagnosis: Nitrofurantoin-induced hepatitis, plus likely nitrofurantoin-induced pulmonary fibrosis.

OUTCOME

Over the following week, the patient's ALT level plateaued and then gradually fell. Her bilirubin and ALT returned to baseline levels over the next 2 months. She is currently being monitored by the respiratory team as an outpatient regarding her pulmonary fibrosis, which will hopefully remain stable or even improve now that the offending drug has been stopped.

CASE DISCUSSION

Nitrofurantoin-associated lung and liver toxicity is a well-documented phenomenon. In patients with acute hepatitis, drug-induced disease should always be considered. Drugs including nitrofurantoin, erythromycin, amiodarone, methotrexate and amlodipine are commonly prescribed, and doctors are not always aware of their potential hepatotoxic side effects.

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CASE 45: VOMITING WITHOUT GASTROINTESTINAL PATHOLOGY

PATIENT HISTORY

A 32-year-old man was admitted from the gastroenterology clinic for intravenous fluid administration. He had been referred to the clinic by his general practitioner 4 weeks earlier for investigation of intermittent vomiting. He gave a 4-month history of feeling nauseated throughout the day, initially associated with vomiting two to three times weekly, but this had since progressed to one to two times daily. There were no clear precipitants such as recent ingestion of food and no relieving factors. He usually vomited either food or bilious matter. There were no features suggestive of regurgitation and there was never any blood or coffee ground matter in the vomitus. There was no associated dysphagia or abdominal pain and his bowel habit remained unchanged. He was unsure how much weight he had lost but said that he was buckling his belt two to three notches tighter than he usually would and his clothes felt very loose. He denied any past medical history and took no regular medications. He worked as a legal aid advisor and lived alone. He had consumed no alcohol since the onset of his nausea and vomiting but did not drink to excess prior to this illness. He had never smoked and did not use recreational drugs.

EXAMINATION

Initial observations: T 36.7°C, HR 98 bpm, BP 100/62 mm Hg, RR 20, SpO₂ 99% on room air.

The patient appeared pale and dehydrated, with dry mucus membranes. He was slim with an estimated body mass index (BMI) of 18. His heart sounds were normal and his jugular venous pressure (JVP) was not visible; there was no peripheral oedema. His chest was clear. The patient's abdomen was soft and non-tender with normal bowel sounds.

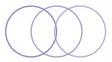
INITIAL RESULTS

Routine blood tests: WCC 7.4, N^o 4.1, Hb 14.2, MCV 84, Plt 266, Na 133, K 3.4, Creat 88, CRP 4, Bili 10, ALT 42, ALP 50, Amylase 47.

DIFFERENTIAL DIAGNOSES

Gastrointestinal tract pathology is the most likely cause of the patient's symptoms. Although regurgitation, which is often a feature of oesophageal pathology, is not present, achalasia will need to be excluded, as will gastric lesions such as pyloric stenosis, malignancy or a hiatus hernia. Peptic ulceration can cause both nausea and vomiting, which may be associated with oral intake (i.e. symptoms worsen immediately post-eating).

Lower gastrointestinal pathology will also need to be considered. Inflammatory bowel disease, particularly Crohn's disease, can present with vomiting, although abdominal discomfort



is usually a feature. Pancreatobiliary disorders, such as cholecystitis or chronic pancreatitis, are less likely to be present in view of the patient's normal liver enzyme and amylase levels.

Next, vestibular causes of vomiting should be considered, particularly as the patient denies abdominal pain or changes to his bowel habit. Further history is needed to establish whether the patient has symptoms of rotational vertigo, hearing loss or unsteadiness, which would be in keeping with inner ear pathologies, such as labyrinthitis or Ménière's disease. The patient should be examined for signs of horizontal nystagmus, which is associated with vestibular or cerebellar disease. The Dix-Hallpike manoeuvre may be performed as a diagnostic aid if benign paroxysmal positional vertigo is suspected.

Elevated intracranial pressure (ICP) due to mass lesions or hydrocephalus is an additional important differential diagnosis to exclude.

Undiagnosed diabetes mellitus presenting with gastroparesis is another possibility. This is delayed gastric emptying due to autonomic dysfunction, particularly vagal nerve damage, secondary to high blood glucose levels. Other metabolic disorders, including hypercalcaemia or thyroid abnormalities, may trigger vomiting.

Lastly, psychiatric disorders, such as anorexia nervosa or bulimia nervosa, or a psychogenic condition should be considered.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

First, this patient is described as clinically dehydrated and will need intravenous fluid replacement. He has a mild hypokalaemia and hyponatraemia, likely secondary to vomiting, and therefore should receive saline with potassium supplementation (e.g. 1 L 0.9% sodium chloride with 40 mmol potassium chloride over 6 hours). Anti-emetic therapy should also be commenced and can be given via the intravenous route initially if the patient is not tolerating oral medication.

Further blood tests will need to be taken, including a blood glucose level (which may be abnormal if diabetes mellitus is present), calcium, magnesium, phosphate, thyroid-stimulating hormone (TSH) and urea levels. If the calcium, magnesium or phosphate levels are low, nutritional supplementation is required.

An oesophago-gastro-duodenoscopy (OGD) will need to be carried out to investigate for potential lesions within the upper gastrointestinal tract. An abdominal ultrasound to investigate for an obstructive lesion, or a computed tomography (CT) head scan to look for a potential cause of elevated ICP, may be performed later, depending on the initial results from the above investigations.

CASE PROGRESSION

The patient was admitted to a medical ward and commenced intravenous fluids and anti-emetics. Glucose, calcium, urea and TSH levels were within the normal range. An OGD was performed, revealing no abnormalities. A CLO test (*Campylobacter*-like organism test; to identify *Helicobacter pylori* infection) was negative. He went on to have an abdominal ultrasound scan, which identified no structural abnormalities.



After 3 days on the ward, the patient had not vomited, nor had he lost any weight. He was receiving regular anti-emetics and was now able to eat regular meals. He was discharged for outpatient follow-up within a fortnight.

Immediately upon discharge, the patient began complaining of vomiting again, possibly due to ceasing regular anti-emetic therapy, although the patient questioned whether there could be a psychogenic cause for his symptoms.

He was re-admitted and a CT brain scan was performed. This showed a 2 cm cerebellar ring-enhancing lesion with surrounding oedema, which was subsequently confirmed on a magnetic resonance imaging (MRI) scan. Corticosteroid therapy was commenced and the patient's nausea settled. A brain biopsy was performed, confirming a glioblastoma multiforme tumour.

Final diagnosis: Glioblastoma multiforme space-occupying lesion causing elevated ICP and subsequent vomiting.

OUTCOME

Chemoradiotherapy was commenced and the patient is being followed up by the oncology team.

CASE DISCUSSION

Raised ICP secondary to a space-occupying lesion is an uncommon cause of vomiting but must be considered once gastrointestinal, biliary and metabolic pathologies have been excluded. Raised ICP may present with headaches, vomiting or seizures, all of which may be worse early in the morning after spending several hours lying flat, which increases ICP. Reduced cerebrospinal fluid (CSF) absorption and a slight elevation in arterial carbon dioxide levels may also occur when sleeping, further exacerbating symptoms of ICP.

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CASE 46: A YOUNG MAN WITH CHEST PAIN

PATIENT HISTORY

A 25-year-old man presented to the emergency department complaining of a 10-day history of worsening central chest pain. The pain was sharp in nature and had come on gradually, with no obvious precipitant, and was worse on deep inspiration. Ibuprofen and aspirin had slightly relieved the pain. The patient felt otherwise well and denied recent illness or trauma. He had no symptoms of cough or shortness of breath. His past medical history included two hospital admissions as a child, where he had been diagnosed with presumed pyelonephritis. Aside from the recent use of non-steroidal anti-inflammatory drugs, he took no regular medications. He was a university student, smoking around five cigarettes each day and drinking 10–12 units of alcohol weekly. He was born in the United Kingdom and his family were of Cypriot origin. He had last travelled abroad 3 years earlier, visiting Honduras and Nicaragua.

EXAMINATION

Initial observations: T 37°C, HR 94 bpm, BP 122/80 mm Hg, RR 20, SpO₂ 99% on room air.

The patient's chest was clear to auscultation, although he was taking shallow breaths. His heart sounds were normal and there was no peripheral oedema. His abdomen was soft and non-tender. A rash was present over the patient's left thigh and shin, which was described as erythematous and macular in appearance.

INITIAL RESULTS

Routine blood tests: WCC 13.7, N^o 12.1, L^o 1.0, Hb 107, MCV 81, Plt 200, Na 138, K 4.5, Creat 81, CRP 64.

Additional blood tests: D-dimer 2.64, TnT 4.

DIFFERENTIAL DIAGNOSES

Inflammation of the pleura, due to underlying autoimmune disease or pulmonary embolism (PE) is one possibility. The patient has pleuritic chest pain and a mild tachycardia, both of which are common features of a PE and he is also slightly tachypnoeic. He has no obvious risk factors for venous thromboembolism (VTE), such as an underlying clotting disorder, malignancy, prolonged immobility, or a recent fracture. The erythematous rash over his leg could be a sign of an underlying deep vein thrombosis (DVT). The team checked his D-dimer level, which is elevated. D-dimer is a fibrin degradation product that accumulates in the presence of thrombus formation. It is important to remember that this does not automatically indicate that a patient has a VTE. There are multiple scoring systems, including the Wells' score, to determine the probability that a patient has a DVT or PE. Generally, when the clinical index of suspicion is high, imaging investigations for DVT/PE should be performed regardless of

the D-dimer level, in addition to commencing anti-coagulation therapy where appropriate. If a DVT or PE is not the most likely cause of the patient's symptoms and they have a low to intermediate risk of VE then a normal D-dimer level is likely to exclude a DVT/PE, i.e. D-dimer has a high negative predictive value.

Pericarditis is another possible cause of pleuritic chest pain. This is inflammation of the pericardial lining and can be caused by certain infections. Viruses, including cytomegalovirus (CMV), HIV, Epstein–Barr virus (EBV) and Coxsackie, and bacteria, including *Mycobacterium tuberculosis* and *Streptococcus pneumoniae*, or fungi, such as *Candida albicans* and *Histoplasma capsulatum*, are known to cause pericarditis, as are autoimmune conditions, such as systemic lupus erythematosus. The pain classically worsens upon lying down and is relieved by sitting forward. In patients with suspected pericarditis, an echocardiogram should be performed to exclude a pericardial effusion, which frequently develops due to the pericardial inflammation. A pericardial effusion may progress to cardiac tamponade, and signs of hypotension, pulsus paradoxus (a large fall in systolic blood pressure during inspiration) and an elevated JVP may be present.

Pneumothoraces cause pleuritic chest pain, but this typically has a sudden onset, which was not the case with this patient. Musculoskeletal pain due to chest wall trauma or costochondritis is a common cause of chest pain in young adults. This diagnosis is more likely if the pain is reproducible on palpation of the chest wall.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

A chest x-ray should be performed to identify possible rib fractures, although the patient denies recent trauma. This will also identify a pneumothorax or pneumonia, if present. A chest x-ray will also allow assessment of the heart size and shape – a globular heart may indicate that a pericardial effusion is present.

An electrocardiogram (ECG) should be performed as soon as possible. Right heart strain, or even the classical S1Q3T3 pattern, may be suggestive of a PE. Saddle ST segments indicate that the patient has pericarditis, while small QRS complexes are suggestive of a pericardial effusion.

A PE is one of the more likely differential diagnoses and therefore if a chest x-ray does not show a cause for the patient's symptoms then imaging in the form of a ventilation/perfusion (V/Q) scan or a CT pulmonary angiogram (CTPA) should be requested. Anti-coagulation therapy, either subcutaneous low molecular weight heparin or an oral anticoagulant, should be administered.

CASE PROGRESSION

The chest x-ray showed very small bilateral pleural effusions. A CTPA showed reactive lymph nodes and sternal sclerosis but no large PE. A V/Q scan was subsequently performed, to identify possible smaller PEs, but this was unremarkable. At this point, approximately 2 days into the patient's admission, he developed worsening chest pain. An ECG showed saddle ST changes across all leads, in keeping with pericarditis (see [Figure 46.1](#)). An echocardiogram was performed, identifying a small pericardial effusion.

Regular ibuprofen was commenced and the chest pain settled, but the patient now complained of pain and swelling of the small joints of his hands. At this point, he was referred to a consultant rheumatologist for review. She spoke with the patient and his parents and established that

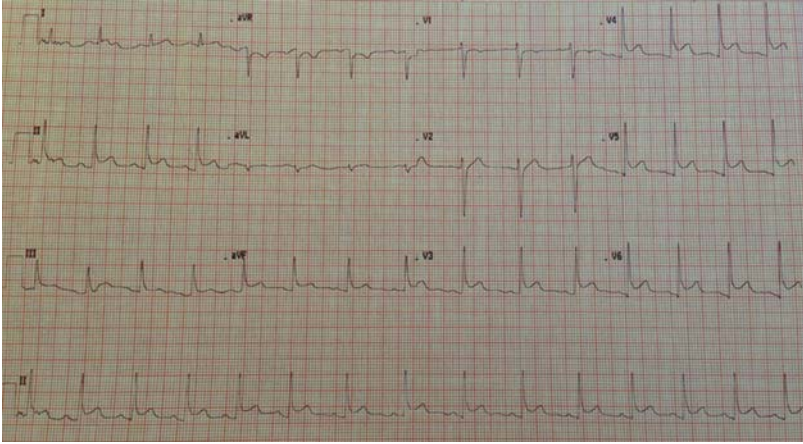
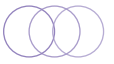


Figure 46.1 ECG showing widespread saddle ST changes.

the possible diagnosis of recurrent pyelonephritis in childhood was based on several admissions to hospital with abdominal pain. His siblings had similar episodes throughout their childhood.

In view of the features of recurrent abdominal pain, pleuritic chest pain, pericarditis and polyarthritis, genetic testing for familial Mediterranean fever was performed. This test came back positive in the patient, and subsequently in his two siblings.

Final diagnosis: Familial Mediterranean fever.

OUTCOME

Once the patient had recovered from the flare-up of familial Mediterranean fever, he was commenced on colchicine, aiming to reduce the generalised inflammation caused by the condition. He represented 4 months later with a further flare-up requiring inpatient care.

CASE DISCUSSION

Familial Mediterranean fever is an inflammatory disorder with an autosomal recessive pattern of inheritance, due to a mutation in the *MEFV* gene. Patients present with a variety of signs and symptoms, including generalised abdominal pain (that may mimic peritonitis), arthritis, pleuritic, pericarditis, fever and rash.

Acute episodes are managed with analgesia, while long-term colchicine is used to prevent further flare-ups. The diagnosis can be challenging to make and is often delayed until the patient has presented on multiple occasions.

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CASE 47: UNILATERAL FACIAL WEAKNESS

PATIENT HISTORY

A 73-year-old man called an ambulance questioning whether he could be experiencing a stroke. He complained of noticing a left-sided facial droop while brushing his teeth 30 minutes earlier and his wife had immediately commented on this a few minutes later. The patient described difficulty closing his left eye and had pain over the left side of his face. He denied any limb weakness and his wife had not noticed any confusion or word-finding difficulties. His past medical history included hypertension and hypercholesterolaemia. He took regular 2.5 mg ramipril OD, 10 mg amlodipine OD and 20 mg atorvastatin OD. He lived with his wife and was independent for all activities. He was a retired casino manager, and an ex-smoker with a 40 pack year history. He drank around 10 units of alcohol per week.

EXAMINATION

Initial observations: T 37°C, HR 82 bpm, BP 138/90 mm Hg, RR 16, SpO₂ 98% on room air.

On inspection, the patient had an obvious left-sided facial droop. A left-sided CN VII (facial nerve) palsy was identified, as indicated by inability to raise the left eyebrow, close the left eyelids tightly, grimace and puff out the left cheek. Taste was not formally assessed. All other cranial nerves were intact. Tone, power, reflexes and sensation were normal in all four limbs. Systems examination was otherwise unremarkable.

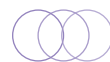
INITIAL RESULTS

Routine blood tests: WCC 12.7, N^o 7.9, Hb 137, Plt 197, Na 135, K 4.2, Creat 66, CRP 24.

DIFFERENTIAL DIAGNOSES

This patient has a unilateral facial nerve palsy, which is typically classified as either an upper or a lower motor neurone lesion. Upper motor neurone lesions are associated with stroke or traumatic brain injury, and can be easily identified as there is sparing of the frontalis muscle (due to bilateral innervation) so the patient is still able to raise both eyebrows and furrow the brow. This patient has a lower motor neurone lesion, which is most commonly caused by an acute or latent infection, with cytomegalovirus (CMV), Epstein-Barr virus (EBV) and HIV being possible causes. A facial nerve palsy secondary to herpes zoster virus is known as Ramsay-Hunt syndrome (or herpes zoster oticus), and is classically identified by a vesicular rash overlying the ear canal or the tongue. Secondary syphilis affecting the facial nerve is a rare but well-documented phenomenon.

Lyme disease is an additional cause of facial nerve palsy and the patient should be examined for evidence of a tick bite or the erythema migrans rash that is associated with this particular infection. Diabetes mellitus, thyroid dysfunction and sarcoidosis are possible non-infectious causes of a facial nerve palsy.



Idiopathic facial paralysis or Bell's palsy is the most common diagnosis for unilateral facial nerve palsy and is a diagnosis of exclusion.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

A panel of blood tests should be sent to identify possible diabetes mellitus (HbA1c and glucose level), thyroid dysfunction (TSH level), syphilis (*Treponema pallidum* serology), HIV, CMV, EBV and herpes zoster virus.

The left ear, tongue and hard palate should be examined for vesicles, indicative of Ramsay-Hunt syndrome. The left eye should be carefully assessed – can the patient close his eye and blink easily? If not, he is at risk of corneal abrasion and the eye should be taped closed.

Bell's palsy has a very good prognosis and patients typically make a spontaneous recovery. Corticosteroids can reduce inflammation around the facial nerve and may increase the chances of recovery if they are administered within 3 days. Anti-viral agents are also often commenced, although there is little evidence that they improve outcomes where no definite viral infection has been identified.

If the patient is well, he can be discharged home for follow-up in the outpatient setting.

CASE PROGRESSION

Oral prednisolone was commenced and the patient's eye was taped shut. Blood results showed a normal HbA1c, a normal TSH and a negative HIV test. The patient was due to be discharged home later that day, but while attempting to mobilise to the bathroom, he complained of dizziness and fell to the floor. He was kept in overnight for observation and the impression was that the loss of vision from his left eye (due to an eye guard being taped in place) was the cause of the fall. The following morning, the patient complained of left ear pain and examination identified multiple vesicles within the ear canal. A diagnosis of Ramsay-Hunt syndrome was made and oral aciclovir therapy was commenced.

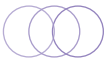
Final diagnosis: Ramsay-Hunt syndrome.

OUTCOME

The patient was followed up in the general medical clinic 4 weeks later and had made a full recovery.

CASE DISCUSSION

Ramsay-Hunt syndrome develops when the herpes zoster virus remains latent within the geniculate ganglion of the facial nerve following an episode of chicken pox infection. The virus may reactivate years later, causing localised symptoms of facial nerve paralysis, a vesicular rash, dizziness and ear pain.



Facial nerve palsy may precede the development of vesicles, as occurred in this case, which may delay the diagnosis. Early treatment with corticosteroid and anti-viral therapy has been shown to improve outcomes. The diagnosis is often missed in patients who do not develop a rash, hence the tendency to start aciclovir in most patients with facial nerve palsy. Indeed, studies have shown that many patients diagnosed with Bell's palsy may actually have herpes zoster or human herpes virus 6 DNA present in their lacrimal fluid, indicative of an acute infection.

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CASE 48: A PATIENT WITH SICKLE CELL DISEASE AND FLU-LIKE SYMPTOMS

PATIENT HISTORY

A 16-year-old man presented to hospital with shortness of breath, fever and headache. He described initially feeling unwell with flu-like symptoms 6 days earlier. Specifically, he felt feverish with an occasional dry cough, lethargy and general malaise. At the time of presentation he had developed shortness of breath on minimal exertion and had a mild frontal headache. He denied both photophobia and neck stiffness. There was no history of chest pain or palpitations. The patient had sickle cell disease with a sickle beta thalassaemia (HbS – β -thalassaemia) phenotype. He took no regular medications, although he was prescribed penicillin V and folic acid. He attended secondary school and had not travelled abroad over recent years. He denied smoking, alcohol intake or recreational drugs. He was not sexually active.

EXAMINATION

Initial observations: T 37.8°C, HR 100 bpm, BP 114/68 mm Hg, RR 19, SpO₂ 99% on air.

The patient looked unwell with obvious pallor and dyspnoea. He was warm to touch, with bounding pulses. His chest sounded clear with no added sounds. His heart sounds were dual and there was no peripheral oedema. His abdomen was soft and non-tender, although the splenic tip was palpable – the patient commented that other doctors had remarked that he had a palpable spleen and that this was therefore not a new finding. He was neurologically intact with no signs of meningism. The patient denied pain when his joints were palpated and there was no joint swelling, no bone pain/tenderness and no rash present.

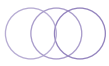
INITIAL RESULTS

Routine blood tests: WCC 3.6, N^o 2.8, L^o 0.7, Hb 32 (baseline 90), MCV 72, Plt 258, Na 137, K 3.7, Creat 50, CRP 88.

DIFFERENTIAL DIAGNOSES

The main abnormality in the above investigations is a very low haemoglobin count, which is an acute change. The patient has sickle cell disease, so it is worth considering several diagnoses that are specific to this condition.

In patients with sickle cell disease, splenomegaly typically develops in childhood due to intrasplenic pooling of sickling cells and higher erythrocyte turnover. In the majority of older children and adults, recurrent episodes of splenic sickling lead to areas of infarction and subsequent splenic atrophy, resulting in ‘autosplenectomy’. Patients with sickle beta-thalassaemia may have persistent splenomegaly. This puts them at ongoing risk of splenic sequestration crises, whereby large volumes of blood pool within the spleen leading to a reduction in circulating erythrocytes. This can present with abdominal pain and an acute, severe



anaemia. Splenic sequestration may also result from immune hyperplasia of the spleen, following an infection such as Epstein–Barr virus (EBV).

Haemoglobin levels can fall acutely during a sickle vaso-occlusive crisis; however, this patient has not presented with symptoms of pain, making this diagnosis very unlikely. The patient will be able to describe what his typical crises are like and whether his sickle cell disease is well-controlled. If symptoms of shortness of breath are present, a sickle chest crisis needs to be excluded as this is potentially life threatening. In this case, however, the patient denies chest pain and has normal oxygen saturations so his shortness of breath can probably be attributed to anaemia.

In younger patients with sickle cell disease, infection with parvovirus B19, which impairs bone marrow function, can lead to an aplastic crisis, due to a pre-existing reduction in erythrocyte lifespan. As red cell production is acutely impaired, a profound anaemia can rapidly develop. A rash over the face and trunk, described as a ‘slapped cheek rash’, is common.

An upper gastrointestinal bleed should be considered as a potential cause of acute anaemia. Has the patient used any medications that could precipitate peptic ulceration, such as non-steroidal anti-inflammatory drugs, e.g. ibuprofen? The history taker needs to establish whether other features of an upper gastrointestinal bleed, such as melaena, are present.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

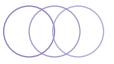
Blood samples should be sent for grouping (‘group and save’) to enable blood transfusion with appropriately matched blood. In this case, the patient has a severe anaemia and is showing signs of haemodynamic compromise, as evidenced by shortness of breath, a mild tachycardia and slight hypotension, all of which are indications for a blood transfusion. A blood film will also be sent to identify haemolysis, although patients with sickle cell disease may have a degree of underlying haemolysis due to abnormal erythrocyte production.

Blood and urine cultures should be taken as part of a septic screen, as well as nasal respiratory virus swabs to identify possible infective causes of the patient’s symptoms. Broad-spectrum antibiotics should be commenced – these can be reviewed and possibly stopped later, once a bacterial infection has been excluded. A chest x-ray must be performed to identify a potential pneumonia. Liver function tests may show an elevated bilirubin level, indicative of increased haemolysis, while an elevated reticulocyte count indicates increased red cell turnover. Serology should also be sent to identify acute cytomegalovirus (CMV), EBV or parvovirus B19 infections.

CASE PROGRESSION

The patient received a 4-unit blood transfusion and his haemoglobin level rose to his baseline level. He was treated for 2 days with intravenous antibiotic therapy, at which point, the serology results came back as positive for an acute parvovirus B19 infection.

The patient developed mild arthralgia over his knees, which initially responded to simple analgesia, but the physical stress of his recent illness triggered a painful vaso-occlusive crisis and he subsequently spent a further 5 days in hospital requiring opiate analgesia.



Final diagnosis: Parvovirus B19 infection triggering an aplastic crisis.

OUTCOME

The patient spent a week in hospital and was then discharged home for community follow-up. His sickle cell disease is well-controlled and he has had no further crises over the following 12 months. The haematology team who usually look after the patient are monitoring his splenomegaly, which will likely resolve as the patient ages. Recurrent splenic sequestration crises may indicate a need for surgical splenectomy, but this patient has had no such episodes.

CASE DISCUSSION

Parvovirus B19 usually affects children, who experience coryzal symptoms and joint pain. A prominent rash often develops, following a period of viral prodrome. A transient reduction in erythropoiesis develops in most patients but usually only becomes clinically significant in patients with pre-existing conditions that result in reduced erythrocyte lifespan, such as sickle cell disease.

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CASE 49: A TEENAGER WITH PALPITATIONS

PATIENT HISTORY

A 19-year-old man presented to the emergency department complaining of palpitations, which had come on 40 minutes earlier. He denied any associated symptoms of chest pain or shortness of breath. He had been experiencing palpitations two to three times per week over the past year, but they had all self-resolved within 5 minutes. He reported seeing a doctor a few months earlier to discuss symptoms of anxiety and panic attacks that he had associated with commencing a university course. He complained of unintentional weight loss and nausea over recent months, which he also felt was due to stress at university. He had no significant past medical history and took no regular medications, although he admitted to occasionally taking an unspecified dose of diazepam, which he had obtained from a relative, when he felt anxious. He had a part-time job in the university bar and drank around 20 units of alcohol per week. He smoked cannabis three to four times per week in addition to around 10 cigarettes per day. He had several recent female sexual partners but reported always using barrier contraception.

EXAMINATION

Initial observations: T 37°, HR 134 bpm, BP 154/78 mm Hg, RR 20, SpO₂ 100% on room air. The patient appeared agitated and diaphoretic. His chest was clear to auscultation. His heart sounds were difficult to hear due to his tachycardia, but there were no obvious murmurs. He had no peripheral oedema. His abdomen was soft and non-tender.

INITIAL RESULTS

Routine blood tests: WCC 6.4, Hb 15.2, Plt 302, Na 137, K 3.9, Creat 62, CRP<1.

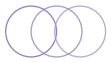
Electrocardiogram (ECG): sinus tachycardia, rate 130 bpm.

DIFFERENTIAL DIAGNOSES

The patient describes symptoms of palpitations, unintentional weight loss and episodes of extreme anxiety. On examination, he is diaphoretic, tachycardic and hypertensive. All of these symptoms and signs could be attributed to an underlying anxiety disorder, but it is important to exclude other important diagnoses first.

Infection is one of the more common causes of tachycardia, but this patient denies symptoms such as a cough, fever or headache and has normal markers of inflammation, making this unlikely.

Hyperthyroidism can present with both tachycardia and hypertension. Graves' disease is the most common underlying condition leading to hyperthyroidism. Patients with hyperthyroidism can also develop symptoms of diarrhoea and heat intolerance.



Excess caffeine intake can stimulate tachycardia, as can excess alcohol. The patient should be asked whether he takes recreational drugs, such as amphetamines, which can induce tachycardia, hypertension and altered mood. Benzodiazepine withdrawal can cause anxiety and tachycardia. If possible, it would be useful to establish how much diazepam the patient was taking in the community and symptoms of withdrawal should be monitored in hospital.

A pheochromocytoma, which is a rare adrenal medullary tumour secreting high levels of catecholamines, can cause hypertension, palpitations and symptoms of anxiety. Patients often describe episodes of diaphoresis, where they sweat excessively, and may notice that episodes increase in frequency over time.

An underlying cardiac arrhythmia, such as atrial tachycardia or Wolff–Parkinson–White syndrome, can be responsible for a driving a tachycardia. This patient has an apparently unremarkable ECG aside from sinus a tachycardia, but when his heart rate decreases, a repeat ECG should be closely inspected to identify potential abnormalities. Uncommon cardiac conditions, such as Brugada syndrome, where abnormal sodium channel function results in tachyarrhythmias should be excluded.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient needs to be examined for the presence of a goitre or exophthalmos, which would support a diagnosis of thyroid disease. The ECG should also be closely inspected for subtle signs of arrhythmia. He is currently stable with no compromise of blood pressure; therefore, treatment does not need to be given immediately.

He should be admitted to a ward where continuous cardiac monitoring can be performed. Blood tests should be sent to assess his thyroid-stimulating hormone (TSH) levels as well as his plasma metanephrine levels (ideally sent on ice) to investigate for a possible pheochromocytoma.

Once some of the initial investigations have returned, the cardiology team may need to be consulted for advice in managing this patient with sinus tachycardia.

CASE PROGRESSION

The patient was admitted under the cardiology team and cardiac monitoring was commenced. His TSH level was within the normal range and he had no clinical signs of thyroid disease. His heart rate was generally 90 bpm, but he had frequent episodes where he developed palpitations and was observed to have a sinus tachycardia of 120–160 bpm. These episodes had settled by the evening and the patient requested that he be discharged home. The cardiology team, however, was concerned that he had remained hypertensive, with an average blood pressure of 154/96 mm Hg since admission, despite normalisation of his heart rate and no obvious anxiety. He was discharged with outpatient follow-up arranged for 1 week later.

When he attended outpatient clinic, the patient was noted to have markedly elevated plasma metanephrine levels, indicative of a pheochromocytoma. A magnetic resonance imaging (MRI) scan of the adrenals was performed – this imaging modality was favoured over an abdominal computed tomography (CT) in this instance to avoid exposing such a young patient to ionising radiation. The MRI scan showed a left-sided adrenal mass, consistent with a pheochromocytoma.



Final diagnosis: Pheochromocytoma.

OUTCOME

The patient was commenced on oral antihypertensive medication to control his blood pressure and several weeks later he underwent a laparoscopic resection of the adrenal tumour. His blood pressure is now controlled without medication and he remains well. His symptoms of anxiety have resolved and he has stopped using benzodiazepines.

CASE DISCUSSION

When attempting to treat hypertension in a patient with a suspected or proven pheochromocytoma, an alpha-adrenergic antagonist, such as doxazosin, is the first-line antihypertensive agent. If a beta-adrenergic antagonist (beta-blocker) is initiated without adequate alpha-receptor blockade, there is a risk of unopposed alpha receptor stimulation, leading to a hypertensive crisis.

Once the pheochromocytoma has been resected, patients may develop a rebound hypotension due to the rapid reduction in circulating catecholamines. Patients are typically advised to consume a high-sodium diet with adequate oral fluids or are given intravenous saline in the immediate perioperative period.

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CASE 50: AN UNUSUAL CAUSE OF HAEMATEMESIS

PATIENT HISTORY

A 39-year-old woman presented to hospital complaining of several episodes of vomiting bright red blood. The haematemesis had begun approximately 24 hours earlier, and she described vomiting three to four times, producing a cupful of blood on each occasion. She complained of a stabbing abdominal pain and repeatedly requested analgesia during history taking. She said the abdominal pain had developed suddenly, 1 day earlier, and was 10/10 in severity. She denied any change in bowel habit and had not noticed any melaena or fresh rectal bleeding. She had felt well until this episode and had no similar problems in the past. She had no past medical history and took no regular medications. She worked as a bank cashier and lived alone. She denied smoking and said she did not ever drink alcohol.

EXAMINATION

Initial observations: T 36.8°C, HR 70 bpm, BP 122/80 mm Hg, RR 16, SpO₂ 100% on room air.

The patient was visibly distressed, complaining of intense abdominal pain. She was warm and well perfused and showed no signs of haemodynamic compromise, with a capillary refill time of less than 2 seconds. Her heart sounds were normal and her chest was clear to auscultation. Her abdomen was difficult to examine due to voluntary guarding throughout and moderate generalised tenderness. Bowel sounds were normal. A digital rectal examination found no signs of melaena or fresh blood. The patient was re-examined following subcutaneous administration of opiate analgesia and her abdomen was found to be soft and non-tender. Shortly after being clerked, the nurses heard the patient vomiting and found her with a bowl containing approximately 50 mL frank blood.

INITIAL INVESTIGATIONS

Routine blood tests: WCC 7.3, Hb 149, MCV 83, Plt 347, Na 138, K 3.6, Creat 72, CRP<1, INR 0.9.

DIFFERENTIAL DIAGNOSES

The patient has had an upper gastrointestinal bleed that has continued since admission to hospital. She also describes severe abdominal pain that developed suddenly and preceded the episodes of haematemesis. A bleeding peptic ulcer or gastric erosion is the most likely cause of her symptoms. Precipitants for this can include an infection with *Helicobacter pylori*, or intake of drugs such as corticosteroids or non-steroidal anti-inflammatory drugs (NSAIDs). Alcohol excess can lead to gastric and duodenal ulceration; however, this patient denies any regular alcohol intake. Ingestion of corrosive substances, as can occur in cases of deliberate self-harm, may be another cause.



The oesophagus may also be the primary site of bleeding. It is unclear whether the patient has experienced previous symptoms of oesophageal reflux or odynophagia. If the patient has had multiple episodes of vomiting, she may have sustained a Mallory–Weiss tear, where there is trauma to the mucosa of the oesophagus. Oesophageal varices, which are dilated sub-mucosal veins, may develop as a result of portal hypertension and are very prone to bleeding.

An oesophageal or gastric malignancy with erosion into a blood vessel should be considered. Further history taking is needed to establish whether the patient has experienced dysphagia or unintentional weight loss.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

Two large-bore intravenous cannulae should immediately be sited to allow rapid resuscitation if the patient becomes haemodynamically compromised. Blood samples should be sent for grouping ('group and save') to facilitate blood transfusion if required.

The patient should be kept nil-by-mouth in case an endoscopy is required and to minimise the risk of further vomiting. An intravenous proton pump inhibitor, such as pantoprazole, should be commenced to reduce gastric acid production.

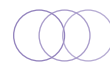
The on-call gastroenterology team should be contacted, as the patient will require an urgent (but not immediate) oesophago-gastro-duodenoscopy (OGD) to investigate the cause of her haematemesis. She is currently haemodynamically stable with a normal haemoglobin level so does not require a blood transfusion at present. She should be closely monitored for further haematemesis or signs of cardiac compromise, such as tachycardia or hypotension.

CASE PROGRESSION

The patient was admitted to a general medical ward where she continued to vomit small volumes of blood, often witnessed by staff. An OGD was performed, which did not identify a cause for her bleeding and no altered blood in her stomach. Her abdominal pain continued and she required increasing doses of morphine. Her haemoglobin level fell slightly over the subsequent days, but she did not require a blood transfusion.

An abdominal ultrasound scan identified no abnormalities. A mesenteric angiogram was being considered as the next step to identify the origin of bleeding. The nursing staff expressed concerns that the patient was frequently away from her bedside, spending time outside the hospital but would complain of severe pain prior to the daily medical ward round, and often experienced haematemesis around this time.

While cleaning her bed space, one of the domestic staff found a blood-stained 20 mL syringe under the patient's bedside cabinet. The patient reported that a junior doctor had left it there while performing phlebotomy earlier. The following day, the patient informed her nurse that the junior doctor had prescribed a one-off ('stat') dose of morphine, which was to be given immediately due to her worsening abdominal pain. The nurse was concerned that the morphine dose was very high and she did not recognise the name or signature of the prescriber. She contacted the on-call junior doctor covering the ward who denied prescribing the morphine. The patient was confronted by the medical and nursing staff and admitted that she had been using syringes to withdraw blood from her intravenous cannula and then feigning



haematemesis and abdominal pain in order to receive opiate medication. She immediately left the hospital, declining further support.

Final diagnosis: Munchausen syndrome/factitious disorder with drug-seeking behaviour secondary to opiate addiction.

OUTCOME

The patient immediately re-presented to another local hospital complaining of abdominal pain and haematemesis. She continued to decline support for her opiate addiction.

CASE DISCUSSION

Opiate-based agents can have highly addictive properties. Patients presenting with opiate misuse may benefit from a range of psychosocial therapies. Some people with dependence on intravenous opiates, such as heroin, receive the pharmacological agent, methadone, which has a relatively long half-life and slow onset of action compared with other opiate-based drugs, thus avoiding positive reinforcement from a 'high' as well as unpleasant withdrawal symptoms such as nausea. Many areas in the United Kingdom have methadone programmes for people who use heroin, to allow daily prescription of methadone with the aim of preventing intravenous drug use and the dangerous behaviours associated with this. The dose of methadone is gradually tapered until the patient has been successfully weaned from opiates.

Munchausen syndrome or factitious disorder is the term given when patients present with feigned illnesses. The underlying reasons for this are varied and often complex. Some patients seek care and support from health professionals, while others may aim to prompt concern or attention from friends and relatives. In some cases, patients will undergo unnecessary procedures, such as a laparotomy or appendectomy following fabrication of severe abdominal pain. Psychosocial support may be beneficial and patients should be referred to see a psychiatry team.

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CASE 51: HEADACHE AND THROMBOCYTOPENIA

PATIENT HISTORY

A 64-year-old woman presented to hospital complaining of worsening headaches. She described a 4-day history of an occipital headache, which she initially noticed soon after waking but was unsure whether the headache itself had woken her. She said the initial pain was around 4/10 in severity but had now reached 8–9/10. There was neither associated neck stiffness, nor any photophobia. The patient denied recent nausea and vomiting. Both paracetamol and ibuprofen slightly relieved the headache. She denied any recent trauma and had not experienced similar headaches in the past. The patient complained of recent difficulty threading a needle and sewing, which she did with her right hand, and said that she felt slightly unsteady on her feet when walking outdoors, which she thought may have been present for the preceding week. Tasks such as holding cutlery and drinking from a cup were not affected. Her past medical history included Sjögren's syndrome, rheumatoid arthritis affecting the small joints of her hands, and hypothyroidism. She took levothyroxine once daily but no other regular medications. She worked as a blood donor carer and lived with her husband and granddaughter. She had never smoked and denied regular alcohol intake.

EXAMINATION

Initial observations: T 36.3°C, HR 58 bpm, BP 138/94 mm Hg, RR 14, SpO₂ 96% on air.

The patient was alert and orientated and appeared well. Her chest was clear to auscultation. An ejection systolic murmur was heard over the aortic region, which did not radiate. Her jugular venous pressure (JVP) was elevated at +5 cm and she had pitting oedema to the mid-calves bilaterally. Her abdomen was soft and non-tender. Neurological examination identified normal tone and power throughout. Upper and lower limb reflexes were brisk bilaterally. Plantars were equivocal. No objective impairment of co-ordination was identified. There were no signs of cerebellar dysfunction and cranial nerves were intact. Photophobia and neck stiffness were not identified.

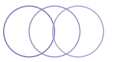
INITIAL RESULTS

Routine blood tests: WCC 6.3, N^o 4.7, Hb 106, Plt 74, MCV 92, Na 140, K 4.0, Creat 80, CRP 3, Bili 12, ALT 13, ALP 113, Alb 41.

DIFFERENTIAL DIAGNOSES

This patient, who has a background of autoimmune disease, presented complaining of headache and loss of fine motor skills in the right hand, while the examination highlighted signs of aortic stenosis and right-sided heart failure. The initial investigations show a mild, normocytic anaemia and a moderate thrombocytopenia.

A cerebral bleed occurring due to thrombocytopenia is one possibility that could explain her neurological symptoms. The thrombocytopenia may be secondary to an underlying



autoimmune condition, such as thrombotic thrombocytopenic purpura (TTP) or idiopathic thrombocytopenic purpura (ITP). TTP leads to increased thrombus formation and if this condition is present, the patient may have developed an ischaemic stroke.

A cerebral venous sinus thrombosis, which develops within the dural sinuses is more common in the presence of chronic inflammatory conditions, such as rheumatoid arthritis, and typically presents with symptoms of headache and focal neurology.

Vertebral or carotid artery dissection may develop spontaneously and presents with headaches and neurological symptoms. Vertebral artery dissection can cause cerebellar ischaemia and subsequent symptoms of impaired co-ordination. Other precipitants for an ischaemic stroke include cerebral vasculitis, which is associated with autoimmune pathology, or a pulmonary embolus with paradoxical emboli formation (cerebral arterial thrombosis due to a pulmonary embolus passing through a patent foramen ovale).

Infective endocarditis can lead to septic embolisation within the central nervous system. This diagnosis could explain the patient's heart murmur and signs of right heart failure, as well as her neurological symptoms.

Meningitis or encephalitis seem unlikely in view of the lack of symptoms such as confusion, photophobia, rash or neck stiffness, as well as the normal inflammatory markers, but these conditions should be considered if the patient deteriorates.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

A blood film should be requested to look for the presence of schistocytes (red blood cell fragments), which are present in patients with TTP and are associated with intravascular thrombus formation.

A computed tomography (CT) head scan should be performed urgently to identify cerebral haemorrhage or ischaemia. If this does not show any abnormalities then a magnetic resonance imaging (MRI) scan should be considered, as this is a far more sensitive test. A lumbar puncture does not need to be performed at present, but should be considered if the patient develops signs of meningitis or encephalitis. If a lumbar puncture is indicated, bear in mind the fact that the patient has a low platelet count and consider discussing the case with a haematologist. The platelet count will need to be re-checked prior to performing any invasive procedure.

An echocardiogram should be carried out to identify any vegetations on the heart valves (indicative of infective endocarditis), which could be responsible for the patient's heart murmur.

CASE PROGRESSION

A CT head scan showed normal appearances of the brain parenchyma. The blood film was reported as showing normal white cell morphology, reduced platelet numbers, and slightly reduced numbers of red cells, some of which demonstrate anisocytosis (unequal size) but no schistocytes. This was felt to effectively exclude the possibility of TTP. The team's plan was to arrange an MRI scan of the brain, followed by a lumbar puncture.

An HIV test was ordered, as well as a full auto-immune screen to identify causes of vasculitis. The patient declined a lumbar puncture, stating that the headache had improved and that she felt hesitant to undergo the procedure. The MRI scan showed small foci of recent infarction in multiple vascular territories. Given the ischaemic infarcts were identified 5 days after the onset of symptoms, she was not referred to an acute stroke service for consideration of

thrombolysis. The patient was commenced on 300 mg aspirin once daily as per current stroke guidance. An echocardiogram showed no obvious vegetations.

The patient's platelet count was re-checked the following day and had fallen to $34 \times 10^9/L$. In view of the low platelet count, further doses of aspirin were withheld. Autoimmune studies confirmed that the patient had Sjögren's syndrome but identified no other underlying conditions. The blood film was repeated – this showed multiple schistocytes, consistent with a diagnosis of TTP. The haematology team confirmed the diagnosis of TTP with an urgent ADAMTS13 test. The patient began a programme of plasma exchange with intravenous methylprednisolone and monoclonal antibody (rituximab) therapy.

Two days later, the patient developed shortness of breath with hypoxia. A CTPA showed large, bilateral pulmonary emboli. Shortly after the scan, she complained of a new right-sided facial droop and mild dysarthria. MRI imaging confirmed progression of the bilateral parietal infarcts.

Final diagnosis: TTP with multiple cerebral and pulmonary infarcts.

OUTCOME

Over the subsequent weeks, the patient continued receiving plasma exchange therapy along with corticosteroids. Her platelet count gradually normalised and she was transferred to a stroke ward for further rehabilitation. She made a good recovery and was discharged home, regaining an independent life.

CASE DISCUSSION

TTP is a clotting disorder, which usually develops due to the development of autoantibodies against the ADAMTS enzyme, which is responsible for von Willebrand factor breakdown. TTP may develop secondary to pregnancy, malignancy or immunosuppressant use, as well as other underlying autoimmune pathologies.

A blood film will usually show red cell fragments and it is unclear why these were not seen on the initial film. Although there are rare case reports of TTP where schistocytes have not been identified, it may be more likely that there was a laboratory error when the film was processed. In this case, haemolytic anaemia was not a major feature and the patient showed no signs of jaundice and did not have an elevated bilirubin level. The patient also remained generally well, while TTP typically causes major morbidity.

TTP can be difficult to distinguish from haemolytic-uraemic syndrome and disseminated intravascular coagulation initially in some cases. Diagnosis is confirmed by the presence of autoantibodies to ADAMTS13. Patients usually require 5–7 days of treatment with plasma exchange and corticosteroids. The anti-CD20 monoclonal antibody, rituximab, may be used in severe disease or refractory cases.

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CASE 52: COFFEE GROUND VOMITING

PATIENT HISTORY

A 57-year-old man was admitted to hospital complaining of several episodes of coffee ground vomiting. He described approximately 10 episodes of vomiting around 100 mL coffee ground matter over the preceding 24 hours. He reported symptoms of light-headedness and weakness, which had come on gradually over the past few hours. He had epigastric pain and complained of 'heart burn' whenever he tried to eat or drink. His past medical history included a hospital admission 6 months earlier with a bleeding duodenal ulcer, which required a laparotomy and a 14 unit blood transfusion. His regular prescribed medications included 20 mg omeprazole OD, which he admitted to only taking around once weekly. He had previously worked as a teacher but had been unemployed over recent years. He admitted to drinking a bottle of vodka (30 units) and smoking 40 cigarettes per day for the past 15 years. He lived alone and had not travelled abroad recently. He had no current sexual partners.

EXAMINATION

Initial observations: T 35.8°C, HR 122 bpm, BP 110/72 mm Hg, RR 20, SpO₂ 88% on room air, 94% on FiO₂ 0.28.

The patient appeared short of breath and uncomfortable. He had dry mucus membranes. He was cool to touch and his jugular venous pressure (JVP) was not visible. His heart sounds were normal and there was no peripheral oedema. His chest was wheezy throughout, but there was good air entry at both bases. His abdomen was soft but slightly tender around the epigastric region, with normal bowel sounds.

INITIAL BLOODS

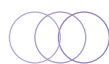
Routine blood tests: WCC 14.2, N^o 11.7, Hb 124, MCV 102, Plt 170, Na 133, K 4.8, Creat 72 (baseline 50), CRP 18, Bili 19, ALT 44, ALP 54, INR 1.1.

DIFFERENTIAL DIAGNOSES

Altered blood in the stomach can have a 'coffee ground' appearance. Given the patient's previous history of a bleeding duodenal ulcer, a recurrence of this is the most probable diagnosis. His haemoglobin level is slightly lower than would be expected and he is tachycardic and hypotensive, all of which may be in keeping with blood loss and subsequent hypovolaemia.

In view of his chronic alcohol misuse, the patient is also at risk of developing liver cirrhosis and secondary portal hypertension, which may result in formation of oesophageal varices. These are dilated sub-mucosal veins in the lower third of the oesophagus, which are very friable and prone to bleeding.

He is also somewhat hypoxic with oxygen saturations of 88% on room air. This may be due to a chronic condition, such as chronic obstructive pulmonary disease (COPD) or it may be



a new problem, such as an aspiration pneumonia, following repeated episodes of vomiting. A simple community-acquired pneumonia may present with vomiting as one of the symptoms, although shortness of breath, fever and cough would likely be more prominent.

Alternatively, the patient may have gastroenteritis and the reported coffee ground vomitus may represent food matter. The patient may also be tachycardic due to alcohol withdrawal and this will need to be closely monitored.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

As with all patients presenting with a high potential risk of bleeding, intravenous access (preferably two large-bore cannulae) should be established and blood samples should be taken for grouping. If there is strong evidence of bleeding or haemodynamic compromise, blood should also be crossmatched.

A blood gas should be taken to assess the patient's oxygenation and ensure he is not retaining carbon dioxide. The blood gas will also give us an immediate estimation of his haemoglobin level and lactate level (a marker of tissue hypoperfusion).

Intravenous fluids should be commenced as the patient appears clinically dehydrated. He should be kept nil by mouth and an intravenous proton pump inhibitor, such as pantoprazole, should be commenced to reduce gastric acid production.

An erect chest x-ray should be requested, to evaluate whether there is a pneumonia present, but also to look for evidence of free air under the diaphragm (signifying abdominal organ perforation) or mediastinal air indicative of oesophageal rupture.

Lastly, this patient has a high alcohol intake and is at risk of withdrawing from alcohol while he is an inpatient. A withdrawal scoring system, such as the Clinical Institute Withdrawal Assessment for Alcohol (CIWA) score, should be carried out regularly to monitor for signs of alcohol withdrawal (tremor, sweating, tachycardia and anxiety) and benzodiazepine medication should be administered, if indicated, to improve the symptoms and reduce the risks of alcohol withdrawal seizures. Patients with chronic alcohol misuse are at risk of severe thiamine depletion and thus may develop Wernicke's encephalopathy, so intravenous supplementation of water-soluble vitamins B (particularly thiamine) and C should be given.

CASE PROGRESSION

Once two large-bore cannulae had been inserted, blood samples were sent for grouping and intravenous fluids and pantoprazole were commenced. The gastroenterology team arranged for an oesophago-gastro-duodenoscopy (OGD) to be performed the following morning to investigate a possible recurrence of peptic ulceration with bleeding, provided the patient remained stable and did not require emergency intervention.

The OGD showed very unusual appearances, which the on-call gastroenterology team had not seen previously. They described a diffuse, circumferential hyperpigmented, almost black, appearance of the upper oesophagus (see [Figure 52.1](#)) and lower oesophagus (see [Figure 52.2](#)) with normal colouration of the gastric and duodena mucosa and several small (<1 cm) areas of ulceration (see [Figure 52.3](#)). The oesophagus appeared very friable and biopsies could not be taken due to the high risk of perforation. The stomach contained fragments of what

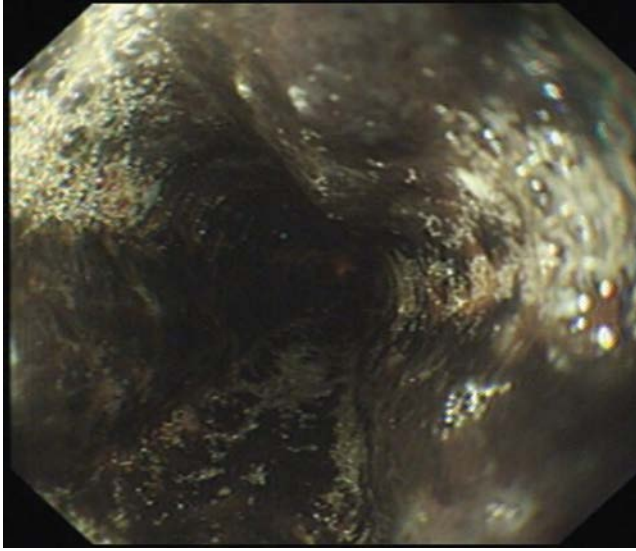


Figure 52.1 Oesophago-gastro-duodenoscopy image showing a hyperpigmented appearance of the upper oesophagus.

appeared to be sloughed off oesophageal mucosa, which was thought to represent the ‘coffee ground’ matter that the patient described vomiting.

The patient was kept ‘nil by mouth’ with intravenous fluids given over the next 24 hours. Causes of pigmented oesophagus were researched, with no clear diagnosis made initially, although oesophageal necrosis was considered to be a possibility. The patient remained haemodynamically stable with no significant change in his haemoglobin level. The OGD

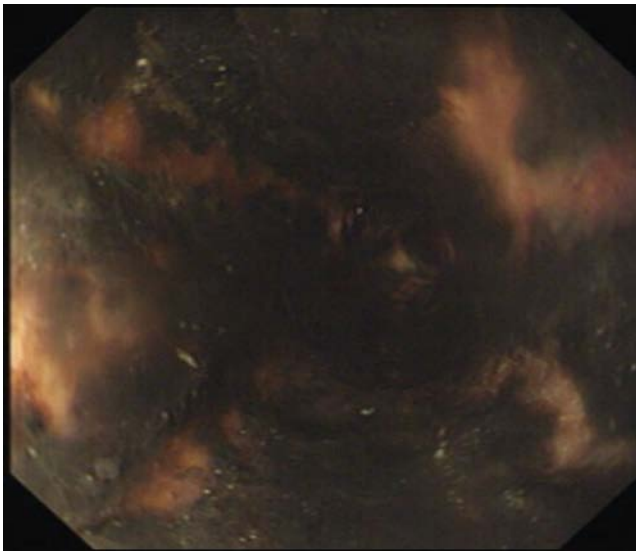


Figure 52.2 Oesophago-gastro-duodenoscopy image showing a hyperpigmented appearance of the lower oesophagus.

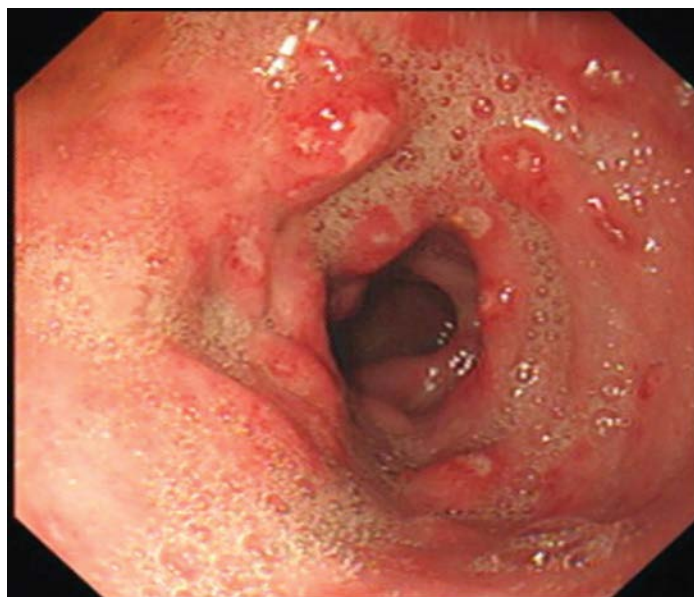


Figure 52.3 Oesophago-gastro-duodenoscopy image showing normal colouration of the gastric and duodena mucosa and several small areas of ulceration.

was repeated 48 hours after the initial one. The appearance of the blackened oesophagus was marginally improved, but the team opted to avoid biopsies once again. After a further 5 days, a final OGD was carried out and the oesophageal mucosa had largely normalised, with only small patches of pigmented tissue remaining. At this stage biopsies were taken, which subsequently confirmed the diagnosis of acute oesophageal necrosis.

The patient made a good recovery and returned to normal oral intake over the following days. Despite several weeks of treatment for alcohol detoxification, he resumed his previous alcohol intake shortly after discharge from hospital.

His oxygen saturations remained low and he was later diagnosed with probable COPD. He was booked to have formal lung function tests as an outpatient.

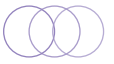
Final diagnosis: Acute oesophageal necrosis.

OUTCOME

The patient was due to be reviewed in the outpatient clinic but failed to attend his appointment. He has not re-presented to hospital, to our knowledge.

CASE DISCUSSION

There are several potential causes of oesophageal hyperpigmentation, including melanocytosis of the oesophagus (where there are increased numbers of melanocytes within the



squamous epithelium), acanthosis nigricans and malignant melanoma, but few causes, aside from acute oesophageal necrosis, that cause a uniformly 'black' appearance.

The oesophagus rarely develops diffuse necrosis, due to its overlapping blood supply from three arteries (branches of the inferior thyroid, thoracic aorta and left gastric arteries). The likely cause of pathology in this case was an upper gastrointestinal bleed leading to hypotension and secondary hypoperfusion of the oesophagus, which may already have been vulnerable following recent major surgery to the region and the chronic exposure to alcohol.

The patient recovered well during his hospital admission, with supportive treatment being given. He is at high risk of further events and it is hoped that he will reduce his alcohol intake with community support.

With thanks to Dr Eleanor Wolffe for her assistance with this case.

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CASE 53: A TEENAGER WITH A RASH

PATIENT HISTORY

A 16-year-old woman presented to hospital complaining of fevers, shortness of breath and a widespread rash. She had been feeling unwell for 4 days with coryzal symptoms and had developed the rash 48 hours before presenting to hospital. She had no past medical history and took no regular medications. She attended secondary school and lived with her parents and two younger siblings. She had received all standard childhood immunisations. She denied alcohol intake and had never smoked or used recreational drugs. She had a boyfriend who was her only sexual partner. She denied recent foreign travel.

EXAMINATION

Initial observations: T 38.7°C, HR 104 bpm, BP 110/68 mm Hg, RR 24, SpO₂ 96% on room air.

The patient appeared dyspnoeic and pale. She was hot to touch and had a dry cough. Her pulses were described as bounding. Heart sounds were normal. There were crackles at both lung bases. She had an extensive vesicular rash over the face, trunk and upper arms, with some lesions appearing to have crusted over, and multiple areas of erythema and excoriation.

INITIAL RESULTS

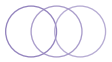
WCC 21.7, N° 15.4, L 5.0, Hb 123, Plt 490, Na 136, K 4.3, Creat 58, CRP 140.

DIFFERENTIAL DIAGNOSES

The patient is clearly unwell with a fever, shortness of breath and a vesicular rash. There are coarse crackles at her lung bases, indicative of pneumonia. Given the patient's preceding symptoms, a viral pneumonia is likely. Varicella-zoster virus (VZV) infection seems probable, given the description of the vesicular rash. The patient and her parents should be asked specifically whether she has had chickenpox previously, as she would be very unlikely to contract this infection twice given the production of antibodies against VZV that occurs following initial infection. Herpes simplex virus (HSV) can also cause a pneumonia, but the patient's rash is not in keeping with this – HSV tends to present with small clusters of vesicles.

Mycoplasma pneumoniae infection can present with a severe pneumonia and typically develops over a time course of days to weeks. A rash is often present, which may be maculopapular initially, but can progress to include vesicular lesions.

Other causes of a widespread vesicular rash include dermatitis herpetiformis; however, this is a chronic condition and is unlikely to be associated with a pneumonia. Fixed drug eruptions can develop in response to a medication allergy – has the patient taken any pharmacological agents recently? The rash is typically maculopapular, but blistering may also be present. Stevens–Johnson syndrome (erythema multiforme major) or toxic epidermal necrolysis (TEN) may develop, both of which are dermatological emergencies associated with respiratory failure.



HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

A chest x-ray should be performed and blood cultures, respiratory viral swabs and swabs of the lesions (bacterial and viral) must be taken to identify the infective organism. If her oxygen saturations fall further, oxygen should be prescribed to target SpO₂ of $\geq 94\%$.

If chickenpox is suspected, the patient should be isolated and barrier nursed in a negative pressure room (if available). Attending staff should have evidence of immunity to VZV. Chickenpox can be particularly dangerous to pregnant women and this patient should have a β -HCG test to ensure that she is not pregnant. An antiviral drug, such as aciclovir, should be administered intravenously. The patient may have varicella pneumonia or could have a secondary bacterial pneumonia and broad-spectrum antibiotics should therefore be commenced.

In case an atypical pneumonia, due to organisms such as *Mycoplasma pneumoniae*, has developed, antimicrobial therapy should include a drug from the macrolide, tetracycline or fluoroquinolone class – this can be discussed with the on-call infectious diseases team. Mycoplasma serology and a urinary legionella antigen should be sent.

CASE PROGRESSION

A clinical diagnosis of chickenpox was made. The patient was isolated in a negative pressure room. Intravenous aciclovir and antibiotics (co-amoxiclav, clarithromycin and a one-off dose of gentamicin) were prescribed. A chest x-ray showed bilateral lung infiltrates and multiple nodular lesions throughout the lung fields ([Figure 53.1](#)), consistent with varicella pneumonia. Over the next 8 hours, the patient became increasingly tachycardic and her blood pressure fell to 80/60 mm Hg. Intravenous fluids were given and the doctors noted that the patient was cool and clammy to touch. Her respiratory rate (RR) increased to 30 breaths per minute

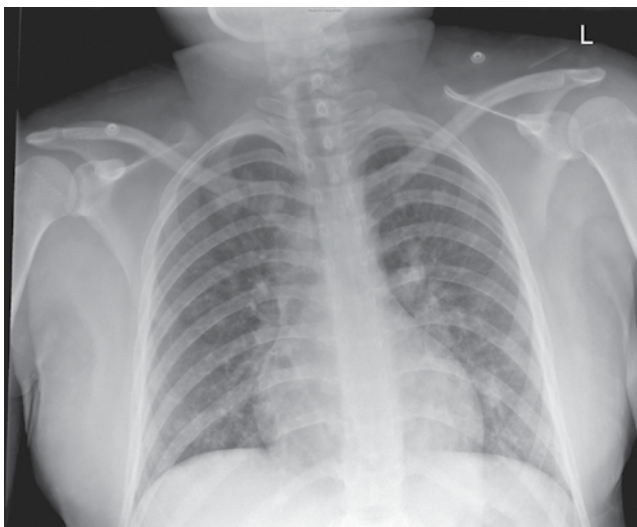


Figure 53.1 Chest x-ray showing bilateral lung infiltrates.



and she required 35% oxygen to maintain oxygen saturations of 96%. She was taken to the intensive treatment unit and required mechanical ventilation for 2 days.

Final diagnosis: Varicella pneumonia.

OUTCOME

The patient made a rapid recovery post-extubation and was discharged home within 5 days of her admission. Her two younger siblings (aged 22 months and 3 years) developed chickenpox during her hospital stay, but they had mild symptoms that were managed supportively at home.

CASE DISCUSSION

While chickenpox is generally a mild, self-limiting disease in young children, teenagers and adults often have a more serious illness and are far more likely to develop complications such as pneumonia or meningoencephalitis. Varicella pneumonia occurs more frequently in smokers and pregnant women.

VZV vaccination is available in the United Kingdom for high-risk individuals, such as those who are immunocompromised or healthcare workers, although more than 90% of adults are already immune to the condition following chickenpox infection in childhood. While vaccination in childhood is effective at producing immunity (>90%), this is not the case in adulthood, with standard effectiveness rates of around 75%. Children are routinely vaccinated against VZV in some countries, including the United States.

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CASE 54: RECURRENT LOWER RESPIRATORY INFECTIONS FOLLOWING A RENAL TRANSPLANT

PATIENT HISTORY

A 43-year-old man presented to the emergency department with a 6-day history of fevers and a cough productive of green sputum. He described feeling fatigued for more than a month and had unintentionally lost around 1 stone in weight over this time. His past medical history included a functioning cadaveric renal transplant 3 years earlier, after developing renal failure secondary to autosomal dominant polycystic kidney disease (APKD). He took regular tacrolimus, mycophenolate mofetil, prednisolone and omeprazole. He worked as a part-time legal secretary. He did not smoke and drank around 6 units of alcohol per week.

EXAMINATION

Initial observations: T 37.8°C, HR 94 bpm, BP 130/82 mm Hg, RR 16, SpO₂ 98% on room air.

The patient appeared comfortable at rest, although he became dyspnoeic following minor exertion. His chest was clear to auscultation and cardiovascular examination was unremarkable. His abdomen was soft and non-tender with a palpable enlarged left kidney. His transplant scar was visible in the right iliac fossa and the transplanted kidney was palpable.

INITIAL RESULTS

Routine blood tests: WCC 18.4, N^o 5.1, Hb 137, MCV 88, Plt 200, Na 138, K 4.1, Creat 92 (baseline 80), CRP 190.

DIFFERENTIAL DIAGNOSES

The patient presents with a 6-day history of fever and a productive cough, preceded by fatigue and weight loss. He has elevated inflammatory markers and is febrile. One of the key parts of the history is that the patient is taking a combination of immunosuppressant drugs, putting him at increased risk of developing infections, including those which people with a healthy immune system are not usually susceptible to.

His symptoms are primarily respiratory in nature, although his chest was clear on examination. A viral pneumonia may have developed. A bacterial pneumonia due to typical pathogens, such as *Streptococcus pneumoniae* or *Staphylococcus aureus*, or atypical pathogens such as *Mycoplasma pneumoniae* or *Legionella pneumophila* may also be present. As the patient is immunocompromised, *Pneumocystis jiroveci* pneumonia (PCP) should be suspected. Pulmonary tuberculosis is also relatively common among people with immunosuppression and would explain the patient's symptoms of weight loss and malaise.

Immunosuppression can additionally increase the risk of developing certain malignancies such as lymphoma.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

A septic screen, including blood and sputum cultures and respiratory viral swabs should be taken. Urine should be sent for routine culture and to be tested for legionella antigen. The patient will need a chest x-ray to identify consolidation or evidence of tuberculosis or malignancy.

If tuberculosis is thought to be likely, the patient should be isolated in a negative pressure room and sputum should be examined for the presence of acid-fast bacilli. Broad-spectrum antibiotics should be commenced, but in view of the complexity of the case, advice should ideally be sought from an infectious diseases specialist to ensure that both typical and atypical organisms are being appropriately treated, as well as PCP if this is suspected.

CASE PROGRESSION

Intravenous co-amoxiclav and oral doxycycline were commenced in view of the high index of suspicion for a pneumonia being present. The patient had a chest x-ray (see [Figure 54.1](#)), which identified a right lower zone cavity with an air-fluid level.

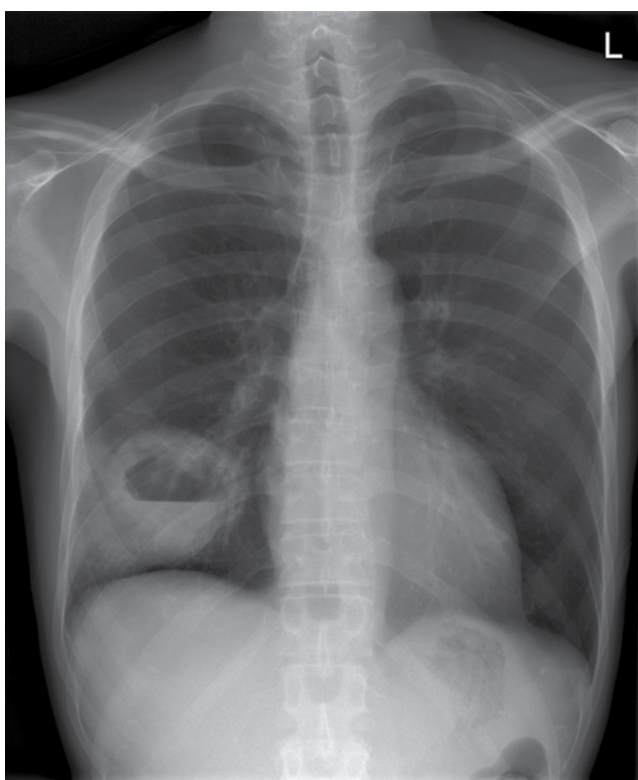
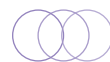


Figure 54.1 Chest x-ray showing right lower zone cavity with an air-fluid level.



A bronchoscopy was performed and bronchial washings and a biopsy were taken, confirming the presence of acid-fast bacilli. A computed tomography (CT) chest scan confirmed the presence of a cavitating lesion with a fluid level present. Anti-tuberculosis therapy (isoniazid, rifampicin, ethambutol and pyrazinamide) was commenced. On advice of the renal team, the tacrolimus and mycophenolate doses were reduced to limit the degree of immunosuppression.

Final diagnosis: Pulmonary tuberculosis with lung abscess formation.

OUTCOME

The patient made a good recovery, although 2 weeks after the immunosuppressant agents were uptitrated, he developed a febrile illness with symptoms of cough again, which was later diagnosed as influenza A infection. He has remained well since.

CASE DISCUSSION

In patients who have undergone a solid organ transplant, it can be challenging to find the balance between preventing graft rejection and putting the patient at risk of infection from immunosuppressant drugs.

Up to 75% of patients with APKD will develop end-stage renal disease by the time that they reach 75 years of age and may require renal replacement therapy (RRT). PKD1 disease tends to advance more rapidly than PKD2. Patients with APKD frequently develop liver cysts and around 5% have evidence of cerebral aneurysm formation on magnetic resonance imaging.

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CASE 55: A HEAVY SMOKER WITH PROXIMAL WEAKNESS

PATIENT HISTORY

A 58-year-old man was admitted to hospital following an episode of collapse in the street. He described stepping out of his car, feeling very light-headed and suddenly waking up on the pavement. His friend witnessed the event and said that the patient lost consciousness for 5–10 seconds and then awoke, without a period of confusion or drowsiness. The patient denied previous episodes of collapse, although he had felt light-headed on standing occasionally over recent days. There was no preceding chest pain or palpitations and the patient did not bite his tongue or lose consciousness. He had no past medical history and took no regular medications. He worked as a long-distance lorry driver and was a current smoker with a 50 pack year history.

EXAMINATION

Initial observations: T 36.8°, HR 72 bpm, BP 144/88 mm Hg, RR 14, SpO₂ 92% on room air.

The patient appeared comfortable at rest. He was warm and well perfused with moist mucus membranes. His chest was generally clear to auscultation aside from a mild expiratory wheeze. His heart sounds were normal and there was no peripheral oedema. The patient had a systolic postural drop of 24 mm Hg. His calves were soft and non-tender with no clinical signs of deep vein thrombosis (DVT). Neurological examination identified proximal weakness with hip flexion, hip extension and shoulder abduction graded at 4/5. All other muscle groups were graded at 5/5 power.

INITIAL RESULTS

Routine blood tests: WCC 7.3, Hb 148, Plt 290, Na 140, K 3.9, Creat 72, CRP 8.

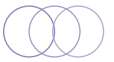
Electrocardiogram (ECG): Normal sinus rhythm, rate 80 bpm.

DIFFERENTIAL DIAGNOSES

This patient has presented following a witnessed collapse, which sounds very much like vasovagal syncope. He has a postural drop despite appearing adequately hydrated. Orthostatic hypotension can develop in the presence of cardiac arrhythmias and valvular disorders, such as aortic stenosis, although this patient has a normal ECG and no audible heart murmurs.

Parkinson's disease and multiple system atrophy may present with autonomic dysfunction, as can type 2 diabetes mellitus. Another possibility is that the patient has a pulmonary embolism. He works as a lorry driver, presumably with long periods of immobility. He has no clinical signs of DVT, however, nor any right heart strain on the ECG.

Specific questions to ask the patient include whether he has found it difficult to walk upstairs and if he is able to stand from a chair without using his arms, to identify a history of proximal



weakness. Thyroid abnormalities can lead to proximal weakness (endocrine myopathy) or polymyositis. If there is a history of recent steroid use, this could trigger a steroid myopathy.

Dermatomyositis is associated with Gottron papules over the extensor surfaces. Is there a history of dark coloured urine (myoglobinuria) indicating rhabdomyolysis?

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

A fluid challenge (e.g. 500 mL 0.9% sodium chloride given over 30 minutes) should be administered to see whether the postural drop resolves, in which case, dehydration would be likely. Creatine kinase (CK) levels (to identify rhabdomyolysis) and serum myoglobin levels should be sent, as well as serum levels of magnesium and calcium. Blood glucose, HbA1c, and thyrotropin (TSH) levels should also be requested.

CASE PROGRESSION

The patient was re-examined by the medical consultant and his signs of proximal weakness remained consistent. TSH, calcium and HbA1c levels were within the reference ranges. A magnetic resonance imaging (MRI) scan of the brain and whole spine revealed no abnormalities.

The neurology team reviewed the patient and noted a mild Trendelenburg gait, signifying weakness of the lower limb abductor muscles. Electromyography was reported as characteristic for Lambert–Eaton myasthenic syndrome.

Final diagnosis: Lambert–Eaton myasthenic syndrome.

OUTCOME

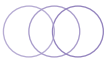
The patient underwent a chest x-ray, followed by a computed tomography (CT) scan of his chest, which identified a speculated mass in the right upper lobe. This was subsequently confirmed to be a small cell lung cancer. The patient commenced chemotherapy shortly afterward.

CASE DISCUSSION

Lambert–Eaton myasthenic syndrome is an autoimmune disorder where antibodies develop against the presynaptic voltage-gated calcium channels (as opposed to myasthenia gravis, which is caused by antibodies against the post-synaptic acetylcholine receptors).

Patients typically present with proximal weakness, primarily affecting the lower limbs. Electromyogram studies classically identify significantly reduced action potentials on repeated stimulation, which subsequently increase dramatically post-exercise.

The condition may develop due to underlying autoimmune disease, in which case, immunosuppression with corticosteroids, intravenous immunoglobulin (IVIg) or plasma exchange may be beneficial. In around 40%–50% of patients, an underlying malignancy is detected – typically small cell lung cancer, but other malignancies, including breast cancer may be seen.



In such cases, Lambert–Eaton myasthenic syndrome is thought to be a manifestation of paraneoplastic syndrome.

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CASE 56: A HILLWALKER WITH FEVER AND CHEST PAIN

PATIENT HISTORY

A 29-year-old man was admitted to hospital following complaints of chest pain. He described left-sided, sharp chest pain, which had come on gradually over 2–3 days. He thought the pain may be worse on deep inspiration and said that he noticed it more when trying to sleep at night. There were no associated features, such as sweating, palpitations or nausea. He complained of a dry cough and flu-like symptoms over the preceding fortnight, with mild swelling of his knees and a rash on his left arm that had now resolved. He worked as a website designer in London and drank around 20 units of alcohol per week. He had never smoked and used no herbal or recreational drugs. He had no recent sexual partners. He had not travelled abroad for several years but did spend most weekends walking in the Scottish Highlands.

EXAMINATION

Initial observations: T 37.4°C, HR 90 bpm, BP 124/86 mm Hg, RR 16, SpO₂ 100% on room air.

The patient looked well and was comfortable at rest. His chest was clear to auscultation and his heart sounds were normal. No pleural or pericardial rubs were heard. His abdomen was soft and non-tender. No rash or joint swellings were observed.

INITIAL RESULTS

WCC 13.8, N° 8.2, L° 4.4, Hb 151, Plt 307, Na 138, K 4.0, Creat 74, CRP 46.

DIFFERENTIAL DIAGNOSES

The patient complains of pleuritic chest pain following an episode of flu-like symptoms. A pulmonary embolism may have developed, although there do not seem to be any risk factors in the history, aside from frequent long-distance journeys to Scotland. The patient should nevertheless be examined for possible signs of a deep vein thrombosis.

A viral infection leading to myo-/pericarditis would appear to be the most likely diagnosis. Patients with pericarditis typically present with pleuritic, positional chest pain, which is exacerbated by lying flat (increased contact between the parietal pleura and visceral pleura) and relieved by sitting forward. Specific viral organisms are often not identified, but common pathogens include adenovirus, Coxsackie virus, Epstein–Barr virus (EBV), cytomegalovirus (CMV), HIV and influenza.

The patient may have a viral pneumonia that arose due to his apparent flu-like illness, or he may have gone on to develop a secondary bacterial infection.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

He will need a septic screen (blood and urine cultures) and, if the patient is able to expectorate sputum, then this should also be sent to the microbiology laboratory for culturing. Respiratory virus swabs should be taken and if there is a high index of suspicion for influenza then the patient should be isolated and barrier-nursed. A chest x-ray will identify consolidation secondary to a pneumonia and may show other useful signs, such as a globular heart, which would indicate that a large pericardial effusion is present.

An electrocardiogram (ECG) should also be performed. Given the likelihood of pericarditis, a transthoracic echocardiogram must be carried out if there is any indication that a significant pericardial effusion is present (e.g. muffled heart sounds and small ECG complexes) or impending cardiac tamponade, such as jugular venous distension, low blood pressure, electrical alternans (the QRS axis alternates between beats due to the heart muscle swinging in the effusion), or pulsus paradoxus (fall in systolic blood pressure by >12 mm Hg during inspiration).

The patient appears clinically well and is haemodynamically stable. Antibiotic therapy may be withheld for now unless evidence of a bacterial infection becomes apparent. Serology should be sent for common viruses that cause pericarditis, including HIV.

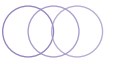
CASE PROGRESSION

A bedside transthoracic echocardiogram was carried out in the emergency department, identifying a small (<5 mm) pericardial effusion, in keeping with pericarditis. Serology did not identify a viral cause for the patient's symptoms.

The patient improved over the next 48 hours. He was due to be discharged home when his partner arrived to accompany him home and showed the junior doctors a photograph of the rash taken 10 days before admission (see [Figure 56.1](#)). The medical team noted the 'bull's eye' rash and, following advice from the infectious diseases team, commenced oral doxycycline



Figure 56.1 Photograph showing a 'bull's eye' rash.



therapy for presumed Lyme borreliosis. Ibuprofen was given regularly for 5 days to treat the pericardial inflammation.

Final diagnosis: Lyme borreliosis.

OUTCOME

The patient was followed up in the outpatient clinic and informed that his serology results were positive for borreliosis. The patient described frequent walks in the Scottish highlands, where he was probably bitten by a tick and subsequently developed an acute disseminated infection, followed by the development of pericarditis.

CASE DISCUSSION

Lyme borreliosis is a bacterial infection (*Borrelia burgdorferi*) that is transmitted via a bite from an infected tick. Around 75% of patients develop an erythema chronicum migrans rash, which may have a 'bull's eye' appearance, several days later. Flu-like symptoms of myalgia, headache and fever may develop at this time. Early complications can include pericarditis, facial nerve palsy, meningitis and first-degree heart block. Later complications are often neurological in nature, such as polyneuropathy, profound fatigue and migraines. Treatment involves oral antibiotics, typically doxycycline or amoxicillin, as well as supportive treatment for complications that may arise.

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CASE 57: A CONFUSED YOUNG MAN

PATIENT HISTORY

A 33-year-old gentleman was brought to the emergency department by his co-workers, who reported a decline in his cognitive function. His manager stated that the patient had initially become emotionally labile several weeks earlier but had more recently developed short-term memory loss and poor co-ordination, frequently tripping over and stumbling when walking, and spilling drinks. The patient denied any symptoms and said he had only consented to come to hospital because he had been escorted by several team members. He said his colleagues were 'going mad' and 'imagining things'. He had no past medical history and did not take any regular medications. He did not smoke, was unclear regarding alcohol intake ('it's none of your business') and denied any recent travel or recreational drug use.

EXAMINATION

Initial observations: T 36.5°C, HR 90 bpm, BP 265/155 mm Hg (similar readings from both arms), RR 18, SpO₂ 99% on room air.

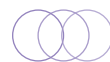
The patient was noted to have an odd affect with emotional lability, becoming intermittently tearful or amused every few minutes. He was alert and orientated to place and person. He was able to name the year and month but could not recall the day of the week. Cardiovascular examination was unremarkable aside from his marked hypertension. His chest was clear to auscultation and his abdomen was soft and non-tender. Neurological examination identified slurring of speech, impaired co-ordination in all four limbs and difficulty following commands. Fundoscopy was challenging as the patient was unable to fully comply with the examination, but the emergency department doctor thought that papilloedema was present bilaterally.

INITIAL RESULTS

WCC 12.9, N° 10.0, Hb 16.5, MCV 88, Plt 257, Na 140, K 3.8, Creat 101, CRP 5.

DIFFERENTIAL DIAGNOSES

The most prominent findings are acute confusion in a young adult along with an extremely elevated blood pressure and probable papilloedema. Papilloedema indicates that raised intracranial pressure (ICP) is present and in this patient with severe hypertension, hypertensive encephalopathy is the most likely diagnosis. The patient may have a history of longstanding undiagnosed hypertension, which has rapidly worsened over several days. The brain is usually able to respond to fluctuations in blood pressure by autoregulating cerebral vasoconstriction or dilatation accordingly to maintain a constant blood flow to the brain. When there is a rapid rise in blood pressure, these homeostatic measures can fail, leading to a change in hydrostatic forces within the cerebral circulation and subsequent development of cerebral oedema. Patients can present with typical features of encephalopathy, including both neurological and psychological dysfunction.



Sympathomimetic agents, such as cocaine and amphetamine, can induce hypertension as well as an altered mental state. The patient should be questioned as to whether he uses recreational drugs or takes other agents that can cause hypertension, such as pseudoephedrine (present in many decongestants) or liquorice (although hypokalaemia would usually be a feature).

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

This is a hypertensive emergency and the patient will need to have his blood pressure reduced rapidly in a very controlled manner. Rapid falls in blood pressure can precipitate organ hypoperfusion, resulting in stroke, renal injury or limb ischaemia, and thus the risk of aggressive therapy causing further long-term damage must be carefully considered.

Intravenous anti-hypertensive agents should be commenced and titrated as an infusion, with close monitoring of the blood pressure via an arterial line. Boluses may be administered if required. Labetalol and sodium nitroprusside are commonly used anti-hypertensive agents in this setting. Once the blood pressure is controlled, oral anti-hypertensive therapy should be commenced and the intravenous infusion gradually weaned.

CASE PROGRESSION

A computed tomography (CT) scan of the brain showed no evidence of haemorrhage or ischaemic injury. The patient was admitted to the high dependency unit where a central venous catheter and a radial arterial line were sited to allow close monitoring of the patient's blood pressure and fluid status. An intravenous infusion of labetalol was commenced and titrated to reduce the mean arterial pressure by 25% over the next 12 hours. The patient's neurological function improved rapidly and his confusion had resolved within 12 hours.

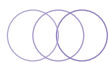
Final diagnosis: Hypertensive encephalopathy.

OUTCOME

After 18 hours in the high dependency unit, the team commenced oral ramipril, amlodipine and bisoprolol and uptitrated these while the labetalol was weaned. At the point of discharge, the patient had a blood pressure of 164/98 mm Hg. He was followed up by a specialist hypertensive department to investigate for possible causes of secondary hypertension and to ensure his blood pressure control and cardiovascular risk factors were optimised.

CASE DISCUSSION

Cases of severe hypertension can be divided into either a 'hypertensive urgency', where no acute vital organ damage (heart, brain or kidneys) is present, or a 'hypertensive emergency', where patients present with acute cardiovascular dysfunction (such as myocardial infarction), neurological dysfunction (encephalopathy, subarachnoid haemorrhage or intracerebral bleeding) or acute kidney injury. A case of hypertensive urgency should be managed by



reducing the mean arterial pressure by around 25% over the first 24 hours to minimise the risk of organ hypoperfusion. Secondary causes, such as hyperthyroidism, phaeochromocytoma and hyperaldosteronism, should be considered in all patients with severe, resistant or early-onset hypertension.

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CASE 58: HAEMOPTYSIS AND RENAL FAILURE

PATIENT HISTORY

A 27-year-old woman presented to the emergency department following an episode of haemoptysis earlier that day. The patient described a 3–4 day history of general malaise and weakness with frequent episodes of shortness of breath on exertion. She was coughing while walking upstairs at work and estimated that she produced approximately 10 mL of frank haemoptysis. She denied previous episodes of haemoptysis or abnormal bleeding when brushing her teeth, opening her bowels or passing urine. She had no past medical history and took no prescribed or herbal medications. She worked as a teaching assistant at an inner-city school and lived alone. She had never smoked. She was of Pakistani origin and travelled to Pakistan every summer for several weeks.

EXAMINATION

Initial observations: T 36.8°C, HR 74 bpm, BP 118/80 mm Hg, RR 14, SpO₂ 97% on room air.

The patient appeared well. She was warm and well perfused and her heart sounds were normal. There were inspiratory crackles at the right lung base. Her abdomen was soft and non-tender.

INITIAL RESULTS

WCC 11.4, N° 8.2, Hb 114, MCV 70, Plt 400, Na 140, K 3.8, Creat 65, INR 1.0, CRP 26.

DIFFERENTIAL DIAGNOSES

The patient presents with a solitary episode of haemoptysis and slightly elevated inflammatory markers with a 4-day history of malaise and shortness of breath on exertion. Bronchopneumonia is the most likely diagnosis, either due to a viral or a bacterial infection. The patient may have contracted pulmonary tuberculosis following travel to Pakistan, from relatives in the United Kingdom, or from exposure at her place of work. London now has the highest rate of tuberculosis infections in Western Europe, with 42 per 100,000 people infected. The prevalence of tuberculosis is high in all major UK cities.

Pulmonary embolism is another cause of haemoptysis that should be considered. The patient has no obvious risk factors, but the history taker should establish when her last long haul flight was, whether she takes the oral contraceptive pill (often not disclosed in the drug history) and if there is a family history of venous thromboembolism.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

A chest x-ray should be performed to look for possible consolidation at the right lung base as well as to identify signs of pulmonary tuberculosis such as a cavitating lung lesion. If the patient can expectorate sputum then this should be sent for culture and microscopy to identify the presence of acid-fast bacilli.

If pulmonary tuberculosis is thought to be likely, the patient will need to be isolated, ideally in a negative pressure room. Broad-spectrum antibiotics should be commenced to cover for possible bacterial community-acquired pneumonia.

Venous thromboembolism prophylaxis (low molecular weight heparin) should be withheld while the patient is monitored for further haemoptysis. Pulmonary embolism seems unlikely at this stage, but focussed history taking will allow further consideration of this.

CASE PROGRESSION

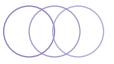
A chest x-ray showed patches of consolidation and increased interstitial lung markings at the right mid and lower zones. Oral co-amoxiclav and doxycycline were prescribed to treat presumed community-acquired pneumonia. The patient was well overnight and was discharged home the following day.

She returned to the emergency department 3 weeks later complaining of nausea and profound fatigue but no further haemoptysis. Repeat blood tests showed that her haemoglobin level had fallen to 84 g/L while her creatinine level had risen to 140 μ mol/L. Her urine dip was positive for 3+ protein and 2+ erythrocytes; although not highlighted at the time, similar findings were seen when the notes from her initial admission were re-reviewed. A repeat chest x-ray showed an increase in interstitial lung markings.

The patient was given intravenous fluids to treat her acute kidney injury and a 2 unit blood transfusion. A renal ultrasound scan was unremarkable. Later that day, a crash call was put out as the patient had experienced large volume haemoptysis estimated to be greater than 800 mL. She was unresponsive but maintained her cardiac output. She was intubated and ventilated and transferred to the intensive treatment unit. Her renal function deteriorated and renal replacement therapy (RRT) (haemofiltration) was commenced.

Anti-glomerular basement membrane (anti-GBM) disease was diagnosed clinically based on the pulmonary haemorrhage and renal failure. Intravenous methylprednisolone and cyclophosphamide were commenced, in addition to plasma exchange. Extracorporeal membrane oxygenation (ECMO – a system of providing external oxygen and carbon dioxide gas exchange) was initiated.

Final diagnosis: Anti-GBM disease.



OUTCOME

The patient made a gradual recovery over the next 10 days, although she continued to receive RRT for a number of weeks. Anti-GBM antibody levels were markedly elevated. Renal biopsy findings were in keeping with anti-GBM glomerulonephritis. The patient was discharged following a prolonged hospital admission. She remains on oral corticosteroid therapy.

CASE DISCUSSION

Anti-GBM disease, also known as Goodpasture's syndrome, is an autoimmune vasculitis where antibodies to the alveolar and glomerular basement membranes develop, leading to pulmonary haemorrhage and glomerulonephritis.

Patients are treated with plasma exchange (plasmapheresis) to remove circulating anti-GBM antibodies. Intense immunosuppression with corticosteroids, azathioprine and cyclophosphamide may be commenced and then gradually tapered in accordance with the patient's response.

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CASE 59: AN UNWELL PET SHOP OWNER

PATIENT HISTORY

A 44-year-old man presented to his general practitioner complaining of general malaise of 1 week's duration and a 2-day history of abdominal pain, diarrhoea and vomiting. He was diagnosed with probable viral gastroenteritis and advised to return if his symptoms persisted. Four days later, he re-presented to the general practitioner with a cough and shortness of breath. His oxygen saturations were 86% on room air and he had crackles at both lung bases. He was brought to hospital by ambulance. His past medical history included gastro-oesophageal reflux disease and seborrheic dermatitis. He took 30 mg lansoprazole once daily only. He lived with his wife and owned a pet shop, in which they both worked. He had never smoked and drank 2–4 units of alcohol per week.

EXAMINATION

Initial observations: T 38.6°C, HR 110 bpm, BP 126/82 mm Hg, RR 22, SpO₂ 86% on room air and 96% on FiO₂ 0.35.

The patient was dyspnoeic and looked unwell. He vomited twice during the examination. He was warm to touch, with bounding pulses. There were bilateral crackles to the mid-zones. Heart sounds were normal and there was no peripheral oedema. His abdomen was soft with mild epigastric tenderness and normal bowel sounds.

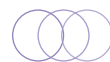
INITIAL RESULTS

Routine blood tests: WCC 21.9, N^o 14.8, L^o 5.6, Hb 149, Plt 388, Na 132, K 3.9, Creat 92, CRP 207, Bili 38, ALT 130, ALP 82, INR 1.2.

DIFFERENTIAL DIAGNOSES

The patient initially had symptoms indicative of viral gastroenteritis and has now re-presented with fever, respiratory failure and elevated inflammatory markers. One possibility is that the patient aspirated during an episode of vomiting and has thus gone on to develop an aspiration pneumonia. Some viral illnesses, such as adenovirus and influenza, can present with features of both gastroenteritis and acute respiratory disease.

Of note, the patient works in a pet shop on a daily basis. Leptospirosis is a bacterial infection that can be contracted following exposure to the urine of infected wild rats. The patient should be directly questioned as to whether he could have encountered wild rats in the days prior to the onset of his symptoms.



HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient will require a full septic screen, including blood, sputum and urine cultures, and a chest x-ray. Vomitus should be sent to test for norovirus. If diarrhoea is present, this should also be cultured. Atypical pneumonias, such as mycoplasma and legionella, should be screened for. Respiratory viral swabs should be taken.

The patient is unwell and septic. Broad-spectrum antibiotics will need to be given as soon as intravenous access is established. An arterial blood gas will identify whether the hypoxia is due to type 1 or type 2 respiratory failure and will provide basic information regarding the patient's acid-base status. A lactate level will also be obtained, which is an essential test in patients with sepsis and yields a significant prognostic value. A lactate level of >4 mmol/L is associated with a high mortality rate. Oxygen should be titrated to $\text{SpO}_2 >94\%$.

CASE PROGRESSION

A chest x-ray showed infiltrates throughout the lung fields. The patient developed hypotension, which did not respond to aggressive intravenous fluid resuscitation. Intravenous co-amoxiclav and gentamicin were commenced. An arterial blood gas showed type 1 respiratory failure with a metabolic acidosis and a lactate level of 5.2 mmol/L.

He was transferred to the intensive treatment unit for inotropic support. On direct questioning, his wife revealed that she and the patient had attended several domesticated rodent and small animal roadshows over the fortnight preceding the hospital admission. Serological testing found no evidence of leptospirosis infection; however, hantavirus was identified.

Final diagnosis: Hantavirus.

OUTCOME

The patient was intubated and mechanically ventilated for 5 days. He made a full recovery and has returned to work.

CASE DISCUSSION

Hantavirus typically infects rodents, particularly wild rats, and can be contracted by humans following contact with their urine or droppings. Pet rats (fancy rats) from established breeders do not carry hantavirus or leptospirosis, but can acquire the infections if they are exposed to wild rodents (e.g. if they come in to contact with their droppings while spending time in their owner's garden). Treatment is usually supportive. Cardiac and pulmonary complications may develop and in these cases, the mortality rate is 30%–40%.

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CASE 60: NECK PAIN AND STERNAL SWELLING

PATIENT HISTORY

A 35-year-old woman attended hospital giving a 2-day history of feeling unwell with intermittent frontal headaches, nausea and generalised weakness. She had vomited once that day. She complained of back and neck pain but denied photophobia. Her past history included depression, bipolar affective disorder and menorrhagia. She was prescribed regular lithium but admitted that she did not adhere to treatment. She lived alone and was not currently working. She injected heroin daily and smoked crack cocaine several times per week. She smoked 20 cigarettes per day and did not drink alcohol.

EXAMINATION

Initial observations: T 38.3°C, HR 105 bpm, BP 142/90 mm Hg, RR 18, SpO₂ 100% on room air.

The patient looked generally well, although she was clammy to touch. Her chest was clear, her heart sounds were dual with no audible murmurs, and her abdomen was soft and non-tender. Kernig's sign was not present, however the patient's neck was stiff on flexion. There was no rash present, although an area of erythema was noted over the sternoclavicular joint. The injection sites appeared clean without evidence of cutaneous infection. There was no point tenderness when the spine was palpated.

INITIAL RESULTS

WCC 19.5, N° 18.5, Hb 110, MCV 97, Plt 278, Na 128, K 3.9, Cr 77, CRP 273.

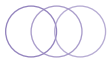
DIFFERENTIAL DIAGNOSES

The patient regularly self-injects heroin and is therefore at risk of skin and soft tissue infections, as well as abscess formation, septicaemia and endocarditis, particularly from *Staphylococcus aureus* bacteria. A spinal abscess or an infection of the sternoclavicular joint is a strong possibility.

There are also features in the history that could indicate meningitis, such as headache, fever and neck stiffness. The patient appears well and has neither rash nor photophobia, but, nevertheless, this site of infection should be considered.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

In addition to a full septic screen, if meningitis or encephalitis is suspected then treatment with intravenous ceftriaxone and acyclovir should be commenced to provide bacterial and viral cover, respectively. Otherwise, antibiotics to cover a *Staphylococcus aureus* infection should be commenced and a lumbar puncture performed. Chest and neck x-rays should be



requested to identify foci of infection. Methadone should be used as required in accordance with local guidance to prevent heroin withdrawal.

CASE PROGRESSION

A computed tomography (CT) scan of the brain showed no acute pathology. The patient consistently refused to undergo a lumbar puncture for the first 48 hours in hospital, as she was concerned about potential pain during the procedure. She was treated with intravenous ceftriaxone for presumed meningitis. On the second day of admission, she developed swelling and increased erythema over the sternum.

Blood cultures taken in the emergency department grew *Streptococcus pneumoniae* in both the aerobic and anaerobic bottles. The patient consented to undergo a lumbar puncture, which showed cerebrospinal fluid (CSF) cell counts and a protein level within the normal range, no pus cells and a gram-negative stain. CSF and plasma glucose levels were 3.8 and 5.8, respectively (CSF glucose levels are typically around 60% of plasma glucose levels and may be markedly reduced in the presence of bacterial, fungal and tubercular infections).

An ultrasound scan of the sternum was not tolerated due to pain over the site. A sternal magnetic resonance imaging (MRI) scan showed left sternoclavicular septic arthritis with adjacent osteomyelitis, soft tissue infection and two superficial abscesses.

Final diagnosis: Septic arthritis of the sternoclavicular joint, likely secondary to intravenous drug use.

OUTCOME

The patient received a 4-week course of intravenous benzylpenicillin. She continued to complain of intermittent back pain and an MRI scan (see [Figure 60.1](#)) was performed, which

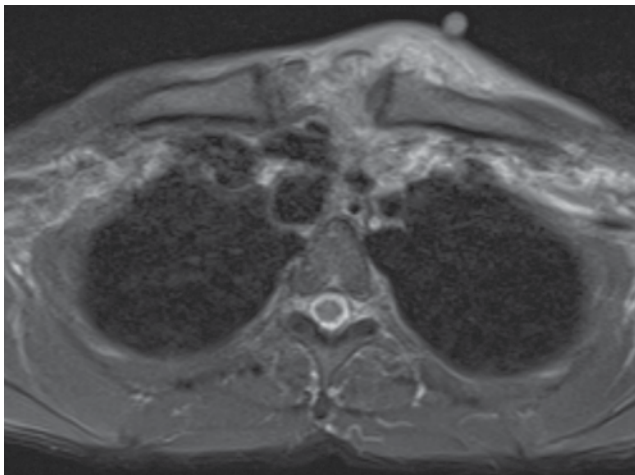


Figure 60.1 Sternal MRI scan showing left-sided sternal osteomyelitis, with overlying soft tissue inflammation.



identified discitis at the level of T5-T6. An echocardiogram was performed to exclude endocarditis and no valvular vegetations were identified.

CASE DISCUSSION

Intravenous drug users (IVDUs) are at increased risk of infections, primarily due to non-sterile injection techniques, which may utilise dirty needles and injection sites that have not been cleaned to remove skin bacteria, thus leading to blood-borne infections. IVDUs who inject sedative agents, such as heroin, are at risk of recurrent episodes of aspiration due to reduced consciousness levels. *Streptococcus pneumoniae* is an organism that colonises the nasopharynx and may have led to a respiratory tract infection in this patient, followed by septic arthritis and discitis due to haematogenous spread.

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CASE 61: FEVERS AND COUGH (PART 1)

PATIENT HISTORY

A 56-year-old man was admitted to the emergency department complaining of a 1-month history of worsening headaches, fevers, lethargy, cough and rigors. He had been deteriorating over recent weeks and had been persuaded by family members to attend hospital. He denied any weight loss or night sweats. His past history was significant for hypertension and recently diagnosed type 2 diabetes mellitus, which was diet controlled. His only prescribed medication was 2.5 mg ramipril OD, although the patient admitted that he did not take this. He was from Nigeria originally and had moved to London 3 years earlier. He visited Nigeria every summer, with his last trip being 9 months earlier, but had not travelled abroad otherwise. He had no unwell close contacts. He had never smoked and did not drink alcohol.

EXAMINATION

Initial observations: T 39.7°C, HR 128 bpm, BP 118/70 mm Hg, RR 32, SpO₂ 98% on room air.

On examination, the patient was tachypnoeic but his chest sounded clear. His heart sounds were normal and there was no peripheral oedema. His mucous membranes appeared dry. His abdomen was soft but generally tender around the epigastric and right upper quadrant areas with 4 cm palpable hepatomegaly present. There was moderate cervical, axillary and inguinal lymphadenopathy present bilaterally – nodes were reported to be soft and approximately 10–150 mm in diameter.

INITIAL RESULTS

Routine blood tests: WCC 13.2, N° 11.2, L° 0.4, Hb 60, MCV 78, Plt 265, Na 137, K 5.9, Creat 230, CRP 55.

DIFFERENTIAL DIAGNOSES

The patient has symptoms of fever and cough, with signs of hepatomegaly and lymphadenopathy. Lymphoma should be considered a likely diagnosis and the patient will need to be urgently investigated for this. Primary lung cancer or an alternative malignancy, such as renal cancer, with pulmonary and/or hepatic metastases, is also possible.

The patient has lived in Nigeria and London, both of which have a high prevalence of tuberculosis. His symptoms of cough, fever and lethargy would be in keeping with a diagnosis of pulmonary tuberculosis. Renal and hepatic involvement may also be present.

He could be experiencing a HIV seroconversion illness, which typically persists for 2–4 weeks. Fever, headache and lymphadenopathy are common symptoms. Alternatively, he could have established HIV with an opportunistic infection and HIV-associated nephropathy.

An infiltrative condition affecting the liver and kidneys is possible, such as sarcoidosis or amyloidosis.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient will need a full septic screen, including a chest x-ray to look for signs of infection (including tuberculosis) or malignancy. Haematinics (iron studies, ferritin, and vitamin B₁₂ and folic acid levels) should be sent to investigate the patient's anaemia. His tachycardia may be attributed to his fever or possibly the underlying anaemia. Two units of blood should be crossmatched and transfused, aiming to bring his haemoglobin level up to 80 g/L.

An arterial blood gas should be performed to assess the patient's oxygen and acid–base status and to identify hyperlactataemia, which is associated with a high risk of mortality.

Ideally a computed tomography (CT) scan of the chest, abdomen and pelvis would be performed initially to aid a diagnosis of lymphoma or tuberculosis, but this should be delayed until the patient is clinically stable, and to avoid the risk of contrast-induced nephropathy. Instead, an ultrasound scan of the kidneys should be performed to rule out obstructive lesions and a fine-needle aspiration of one of the palpable lymph nodes should be scheduled to obtain a tissue diagnosis.

CASE PROGRESSION

After 24 hours of intravenous fluids (0.9% sodium chloride), the patient's tachycardia had resolved, although he was persistently pyrexial. A lumbar puncture was carried out to exclude meningitis secondary to tuberculosis or a viral infection, and this was essentially normal.

His renal function improved slightly, with the creatinine level plateauing at 170 $\mu\text{mol/L}$. A CT scan of the chest, abdomen and pelvis showed generalised, large volume lymphadenopathy, making lymphoma and tuberculosis the main differential diagnoses. The haematology team reviewed the patient and performed bone marrow aspirate and trephine (BMAT) sampling. A cervical lymph node was also excised. The results of these tests excluded lymphoma.

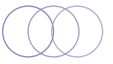
Eight days after his admission, an HIV test came back as positive with a low CD4 count of 9 (reference range 450–1660 cells/mm³) and a viral load of 100,000 copies/mL. The lymph node that was biopsied had moderate numbers of acid-fast bacilli present and anti-tuberculosis treatment was commenced.

A renal ultrasound showed appearances consistent with an infiltrative process. The renal team reviewed and considered that the renal impairment could be due to either renal tuberculosis or HIV-associated nephropathy.

Final diagnosis: Tuberculosis and HIV co-infection.

OUTCOME

The patient was discharged home with an appointment for the HIV outpatient clinic, where anti-retroviral therapy would be considered.



CASE DISCUSSION

Tuberculosis is the most common opportunistic infection and the leading cause of death in patients with HIV. HIV is a major risk factor for latent tuberculosis transforming to active disease and thus all patients with a new diagnosis of tuberculosis should be tested for HIV. There was a delay in testing for HIV in this case, partly due to the patient assuring the team that he was unlikely to be at risk of the infection when testing was discussed.

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CASE 62: CHEST PAIN AFTER BAD NEWS

PATIENT HISTORY

A 59-year-old woman was brought to hospital complaining of chest pain. The pain was central and crushing in nature, radiating to her left arm and jaw. She felt short of breath and nauseated. The pain began approximately 30 minutes earlier. Her past medical history was only significant for a gastric ulcer 5 years earlier. She took 20 mg omeprazole OD only. She worked as a journalist and had never smoked. Upon asking about her family history, the patient became very distressed, explaining that her husband had died in an accident 2 days earlier.

EXAMINATION

Initial observations: T 37°C, HR 80 bpm, BP 138/84 mm Hg, RR 18, SpO₂ 98% on room air. Systems examination was unremarkable.

INITIAL RESULTS

Routine blood tests: WCC 8.2, Hb 133, Plt 207, Na 140, K 4.0, Creat 68, CRP 2.

DIFFERENTIAL DIAGNOSES

The patient presents with central crushing chest pain following recent intense emotional distress. The most probable diagnosis is acute coronary syndrome (ACS) where coronary artery ischaemia leads to unstable angina or myocardial infarction. Myocardial ischaemia develops when the oxygen demand from the cardiac muscle is greater than the oxygen supply. Triggers can include emotional stress, due to the release of catecholamines and subsequent tachycardia and hypertension.

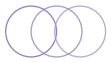
Aortic dissection classically presents with tearing chest pain that radiates to the back. Hypertension may be a prominent feature in cases of proximal dissection. Although the patient's history is not typical for aortic dissection, this is a condition with a high mortality and needs to be excluded.

The patient suffered from peptic ulcer disease several years ago and her chest pain may therefore be attributed to gastro-oesophageal reflux disease or gastric ulceration.

Lastly, anxiety attacks frequently have features of chest pain, dyspnoea and nausea. The above pathologies should be excluded before arriving at this diagnosis.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient should be treated for presumed acute coronary syndrome. An electrocardiogram (ECG) may show ST segment elevation, in which case an ST-elevation myocardial infarction (STEMI) will be diagnosed and the patient will be given high-dose anti-platelet therapy and



assessed for eligibility to undergo reperfusion treatment with percutaneous coronary angioplasty. If there is no ST elevation, the patient will be managed with dual anti-platelet therapy and low molecular weight heparin. Serial ECGs should be performed to assess for the development of ischaemic features, such as ST-depression or T wave inversion, and to monitor for dynamic changes.

Analgesia, typically morphine sulphate, should be offered, plus an anti-emetic agent. Glyceryl trinitrate (GTN) spray should be administered to vasodilate the coronary vessels and relieve chest pain. An intravenous infusion of GTN may be required if the pain persists. Troponin T or I levels should be monitored, as a rapid elevation indicates the presence of myocardial damage.

CASE PROGRESSION

An initial ECG showed T wave inversion in leads II, III and aVF, indicative of inferior myocardial ischaemia. An initial troponin T level was 36 ng/L (reference range 0–14 ng/L). The patient received 300 mg aspirin, 300 mg clopidogrel and low molecular weight heparin (enoxaparin dose of 1.5 mg/kg). She was given 10 mg morphine sulphate intravenously and her pain settled.

The troponin T level rose to 124 ng/L 12 hours after the pain developed. She was taken to the cardiac catheter laboratory later that day, but coronary angiography revealed normal coronary arteries with minimal atherosclerosis and no evidence of stenosis. An echocardiogram showed impaired left ventricular systolic function with an ejection fraction of 30%, left ventricular wall motion defects and apical akinesis. She developed severe pulmonary oedema requiring intravenous diuretics, which led to profound hypotension. She was transferred to the coronary care unit where she received a dobutamine infusion and then to the intensive treatment unit where she received inotropic support and an intra-aortic balloon pump was sited.

She made a rapid recovery over the next 3 days and was discharged home 10 days later. A subsequent echocardiogram showed complete recovery of the apical and left ventricular function with an ejection fraction of 50%–60%. She was diagnosed with Takotsubo cardiomyopathy.

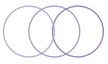
Final diagnosis: Takotsubo cardiomyopathy.

OUTCOME

The patient has had no further recurrence of symptoms and has now been discharged from the outpatient clinic.

CASE DISCUSSION

Takotsubo cardiomyopathy is a condition presenting with chest pain and signs consistent with acute coronary syndrome but no underlying coronary artery stenosis. Around 75% of patients have experienced an episode of major emotional or physical stress in the preceding



hours or days. There is classically a transient impairment of left ventricular function and atrial ballooning that resolves over a time course of weeks.

The underlying pathology is unclear, although possible contributing factors may include an increase in catecholamine release leading to myocardial stunning and/or spasm of the coronary arteries or vessels within the myocardial microvascular bed.

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CASE 63: A YOUNG WOMAN WITH CHEST PAIN

PATIENT HISTORY

A 19-year-old woman presented to the emergency department complaining of a 4-day history of epigastric and central chest pain. The pain was stabbing in nature and came on in waves of severe intensity. She had vomited twice and complained of odynophagia. She was very tearful and unable to give further details regarding the pain. She was a politics student and lived in university halls of residence. She smoked 10 cigarettes daily and used cocaine at the weekend. She drank around 20 units of alcohol per week, although this was typically all consumed over Friday and Saturday nights.

EXAMINATION

Initial observations: T 39°C, HR 110 bpm, BP 108/74 mm Hg, RR 20, SpO₂ 100% on room air.

The patient appeared distressed but generally well. There was mild, generalised abdominal tenderness, but bowel sounds were normal. Systems examination was otherwise unremarkable.

INITIAL RESULTS

Routine blood tests: WCC 11.1, N° 9.4, L° 1.5, Hb 137, Plt 289, Na 130, K 3.5, Creat 68, CRP 151.

DIFFERENTIAL DIAGNOSES

Acute coronary syndrome needs to be considered despite the patient's young age. She regularly uses cocaine, which can induce coronary vasospasm and symptoms of myocardial ischaemia that can progress to myocardial infarction.

A peptic ulcer and/or gastro-oesophageal reflux disease can cause symptoms of severe chest pain ('heart burn') and is more common in smokers and people who drink alcohol to excess or binge drink.

Oesophageal spasm can present with non-cardiac chest pain whereby uncoordinated or excessive oesophageal contractions lead to chest and epigastric pain associated with odynophagia. A food bolus is another possibility, when a piece of food (typically steak or other thick cuts of red meat) causes oesophageal obstruction. Patients have chest and/or neck pain and often retch and regurgitate food. In severe cases, patients are unable to even swallow their own saliva and require intravenous fluid hydration until the bolus passes or is mechanically removed.

If the patient has been vomiting forcefully prior to the pain she may have developed an oesophageal rupture, which is a medical emergency requiring surgical intervention.



HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

An electrocardiogram (ECG) should be performed to identify signs of cardiac ischaemia. A troponin T or I level should be checked as an elevation would point toward coronary vasospasm. The patient should be questioned as to when she last used cocaine, as well as when and what she last ate and whether she recalled food becoming stuck in her oesophagus.

A chest x-ray may show signs of oesophageal rupture, such as subcutaneous emphysema, hydrothorax or subdiaphragmatic air. The patient should be kept nil-by-mouth in case an endoscopic or surgical intervention is required. Intravenous fluids and a proton pump inhibitor should be prescribed. In view of the patient's fever, blood and urine cultures should be taken.

CASE PROGRESSION

The patient remained distressed and tearful, making further history taking difficult. She required frequent doses of morphine for her chest and epigastric pain. She began to complain of shortness of breath and worsening odynophagia. Her CRP peaked at 250 g/L and intravenous co-amoxiclav was started to treat an infection of unknown source. An abdominal ultrasound scan was unremarkable.

She was re-examined and an abdominal bruit was thought to be heard. A magnetic resonance angiography (MRA) scan of the aorta was performed to look for signs of aortitis, which was the working diagnosis at the time, but no large vessel vasculitis was identified. An oesophago-gastro-duodenoscopy (OGD) was requested to investigate for possible oesophagitis and/or gastritis. As the OGD was attempted, it was noted that the patient's oesophagus was intermittently spasming.

Final diagnosis: Diffuse oesophageal spasm with underlying infection.

OUTCOME

After 8 days in hospital, the patient's symptoms gradually resolved and her fever settled. She did not require further treatment and has not re-presented to hospital.

CASE DISCUSSION

Diffuse oesophageal spasm can present with moderate–severe chest pain, often mistaken for angina. Patients may have acute presentations or may develop chronic oesophageal spasm. Symptoms include odynophagia, regurgitation and vomiting. Acute viral infections are thought to be possible triggers for the onset of achalasia and diffuse oesophageal spasm. Glyceryl trinitrate and calcium channel antagonists may provide symptomatic relief.

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CASE 64: RECURRENT EPISODES OF HYPOGLYCAEMIA

PATIENT HISTORY

A 40-year-old man was brought to the emergency department after being found unconscious at home. His girlfriend reported that the patient had been well beforehand with no recent illnesses and no previous episodes of collapse. He was not taking any regular medications. He worked as a barman in a local pub. No further history was available at this time. The ambulance crew reported that he had a capillary glucose level of 1.4 mmol/L on arrival.

EXAMINATION

Initial observations: T 35.8°C, HR 96 bpm, BP 110/70 mm Hg, RR 24, SpO₂ 98% on room air.

The patient was unresponsive, with a Glasgow Coma Scale (GCS) score of 6 (E1V1M4). His pupils were equal and reactive to light. There were no signs of head injury, rash, bruising, tongue biting or urinary incontinence. Heart sounds were normal and his chest was clear. His abdomen was soft.

INITIAL RESULTS

Routine blood tests: WCC 6.2, Hb 146, Plt 281, Na 142, K 3.8, Creat 142, CRP 2, plasma glucose 2.6 mmol/L (after treatment with glucagon and intravenous dextrose solution with the ambulance service).

DIFFERENTIAL DIAGNOSES

The patient presents with reduced consciousness due to hypoglycaemia and is unable to provide further history. Has the patient taken an overdose of insulin or oral hypoglycaemic agents as a form of deliberate self-harm or attempted suicide? Overdoses of beta-blockers and haloperidol can also cause hypoglycaemia.

His partner reports that he is normally fit and well with no past medical history, but he may not have revealed a diagnosis of diabetes mellitus. He may have accidentally overdosed on insulin or oral hypoglycaemic agents or be fasting/reducing his oral intake while using these drugs. The patient has an elevated creatinine level, which could be due to either an acute or chronic kidney injury. If his renal function has acutely worsened, there may be impaired metabolism of renally excreted drugs, such as certain sulphonylurea-based agents.

He may have an insulinoma, which is a neuroendocrine tumour of the beta islet cells of the pancreas. Patients present with recurrent episodes of hypoglycaemia and surgical resection of the tumour is typically performed.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient is unable to protect his airway and is likely to require intubation. He should continue to receive a high concentration dextrose infusion and once his glucose level is stable at



>4 mmol/L, a 5% dextrose solution can be commenced. Remember to take a plasma glucose level as well as capillary glucose readings initially as these are more accurate and not susceptible to falsely elevated readings due to sugar on fingers.

If the patient does not become more alert following normalisation of his glucose level, a computed tomography (CT) scan of his head should be performed to identify potential catastrophic events such as a stroke or a haemorrhage.

CASE PROGRESSION

Over the next 5 minutes the patient's blood glucose level rose to 4.6 mmol/L and he awoke. He was initially confused and aggressive but gradually became alert and orientated. He denied using any medications or taking recreational drugs and confirmed that he had no past medical history. He stated that he used creatine supplements to support his training at the gym, which was thought to explain his elevated serum creatinine. He was taken to the medical ward for further monitoring. Over the next 24 hours, his capillary glucose levels were 4–6 mmol/L and the patient remained well. Pro-insulin and C-peptide levels were taken to investigate for a possible insulinoma.

The patient was due to be discharged later that evening but was found collapsed and unresponsive in bed by his nurse. Again, his capillary glucose level was <1.5 mmol/L and he was taken to the intensive treatment unit for further monitoring. He responded well to intravenous dextrose and glucagon therapy but remained somewhat disorientated for several hours. He returned to the medical ward the following day. His belongings and bed space were searched during his second collapse and no insulin or oral hypoglycaemic agents were seen. His blood glucose levels were stable over the next 2 days. Once again, immediately prior to discharge, the patient collapsed with hypoglycaemia. At this point, results of a urine drug screen came back as positive for sulphonylurea medications.

Final diagnosis: Sulphonylurea-induced hypoglycaemia.

OUTCOME

Upon direct questioning, the patient's partner admitted to poisoning him by administering gliclazide with his food. The police were subsequently involved.

CASE DISCUSSION

Patients with oral hypoglycaemic toxicity should be observed for at least 12 hours to ensure their blood glucose levels remain stable. Most patients will make a full recovery without long-term complications.

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CASE 65: RAPIDLY PROGRESSIVE DEMENTIA

PATIENT HISTORY

A 66-year-old man presented to hospital following a fall at home. He recalled tripping over a rug and falling onto his left side without sustaining a head injury. His wife accompanied him and described two additional falls at home over the preceding week. She asked to speak privately with the junior doctor and said that she had become increasingly concerned about her husband in recent weeks. He had been irritable and had been asked to leave his job following an argument with his boss. He had been struggling to remember the names of his children, forgetting to turn the gas off after cooking and losing his belongings. One week earlier, she had found him sitting in the front garden as he could not remember how to open the front door. She also thought that he may be occasionally responding to auditory hallucinations. Until 6 weeks ago, he had been fit and well. His past history included hypertension and diet-controlled type 2 diabetes mellitus. He took losartan for his hypertension and a multivitamin each day. He worked as a senior manager at a building society until recently. He did not smoke and typically drank around 8 units of alcohol per week, although his wife reported that this had increased recently.

EXAMINATION

Initial observations: T 36.8°C, HR 70 bpm, BP 130/90 mm Hg, RR 16, SpO₂ 98% on room air.

There were no obvious injuries sustained in the fall and the patient denied any pain. His speech was slurred and he appeared agitated. Cardiovascular, respiratory and abdominal examinations were unremarkable. Tone was mildly increased in the upper limbs and reflexes were diminished. A resting tremor was present. His abbreviated mental test score (AMTS) was 7/10 and he was noted to be distractible and irritable. His gait was ataxic with impulsive, clumsy movements.

DIFFERENTIAL DIAGNOSES

Alzheimer's disease is the most common cause of dementia, although it usually progresses slowly over a course of years, beginning with memory loss. Lewy body dementia may progress more rapidly with significant deterioration over several months; patients present with fluctuations in cognition and Parkinsonian features, such as a shuffling gait and cogwheel rigidity.

Sporadic Creutzfeldt–Jacob disease is a prion disease that causes a rapidly progressive dementia along with neurological impairment that usually results in death within a year.

HIV dementia and central nervous system (CNS) malignancies are other causes of progressive cognitive impairment that should be considered. Although unlikely in this case, it is important to remember that depression may present with signs of early dementia.



HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

A computed tomography (CT) brain scan should be performed urgently to identify possible pathologies such as an intracerebral bleed, evidence of hydrocephalus or a space-occupying lesion. Small vessel disease may indicate that vascular dementia is present. Depending on the results of the CT scan, a magnetic resonance imaging (MRI) brain scan will usually be the next step to obtain more detailed views of the CNS.

Blood tests should be carried out to exclude common causes of confusion, including HIV and syphilis tests, vitamin B₁₂ and folate levels, a corrected calcium level and thyroid function tests.

CASE PROGRESSION

A CT scan was requested, but the case was discussed with the radiology team who felt that an MRI brain scan was a more appropriate initial investigation. This was reported as showing widespread cortical atrophy and Alzheimer's dementia was thought to be probable. The patient was discharged home for community follow-up.

Three weeks later, his condition had deteriorated and he was experiencing both auditory and visual hallucinations. His wife reported that he had been unable to sleep for more than 30 minutes at a time. The patient was admitted to hospital where examination identified worsening tremor in both upper limbs and frequent myoclonic jerks. A repeat MRI scan showed worsening cerebral atrophy with high signal intensity in the caudate nucleus. A lumbar puncture was performed. The opening pressure was 16 cm H₂O (reference range 10–20 cm H₂O), the cell count, glucose level and protein level were unremarkable and viral polymerase chain reaction (PCR) did not identify an infective source. Oligoclonal bands were not present. The cerebrospinal fluid (CSF) 14-3-3 protein level was elevated, indicative of Creutzfeldt–Jakob disease.

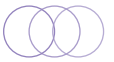
Final diagnosis: Sporadic Creutzfeldt–Jakob disease.

OUTCOME

The patient continued to rapidly deteriorate over the following weeks. His speech became unintelligible and he had frequent tonic–clonic seizures. Six months after his initial presentation, his care was transferred to a hospice where he subsequently died. A post-mortem brain biopsy confirmed Creutzfeldt–Jakob disease.

CASE DISCUSSION

Sporadic Creutzfeldt–Jakob disease is a rare prion disorder that typically develops in the seventh and eighth decades of life. Features include a rapidly progressive dementia, speech disturbance, myoclonus and hallucinations. Diagnosis may initially be difficult as the early stages of the disease share features of Alzheimer's dementia and Lewy body dementia. MRI



scans of the brain may show high signal intensity at the putamen and/or caudate nucleus, along with cortical atrophy. CSF 14-3-3 protein levels may be elevated in Creutzfeldt–Jakob disease, but definitive diagnosis is made following a biopsy of brain tissue. As yet there is no specific treatment for Creutzfeldt–Jakob disease and the main goal is to control symptoms and ensure patients remain comfortable.

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CASE 66: NEW CONFUSION IN A PATIENT WITH BIPOLAR AFFECTIVE DISORDER

PATIENT HISTORY

A 52-year-old man was brought to hospital after being found wandering in a state of distress by concerned passers-by. He described feeling disorientated and aware of a threat to his safety, although he was unable or unwilling to elaborate further. He said that his past medical history included bipolar affective disorder and hypertension. He took 350 mg lithium carbonate (modified release formulation) OD and had recently commenced 2.5 mg bendroflumethiazide OD to treat his newly diagnosed hypertension. He lived alone and worked part-time in a consultancy firm. He denied drinking alcohol and had never smoked. He had previously attended regular community mental health drop-in sessions but said that he no longer did so as his bipolar affective disorder had been stable for years.

EXAMINATION

Initial observations: T 37.2°C, HR 76 bpm, BP 138/93 mm Hg, RR 14, SpO₂ 99% on room air.

The patient appeared agitated but otherwise well. No abnormal findings were identified during respiratory, cardiovascular or abdominal examinations. Neurological examination identified a tremor in all four limbs, symmetrically increased tone in the lower limbs and an extrapyramidal gait.

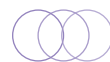
INITIAL RESULTS

Routine blood tests: WCC 8.8, Hb 127, MCV 94, Plt 260, Na 132, K 4.6, Urea 15.8, Creat 160 (2 years earlier, baseline was 84), CRP 5.

DIFFERENTIAL DIAGNOSES

The patient has impaired renal function compared with baseline, which meets the criteria for an acute kidney injury (creatinine rise to >150% baseline). His renal failure may have led to the development of lithium toxicity, as lithium is primarily cleared via the kidneys. Commencing bendroflumethiazide may have caused or contributed to impaired renal function, thus reducing lithium clearance. Additionally, bendroflumethiazide can cause hyponatraemia, which increases lithium reabsorption from the proximal tubules.

Chronic alcohol misuse and poor nutrition can lead to Wernicke's encephalopathy presenting with acute confusion, ataxia and delirium tremens, encephalitis should also be considered as a possible cause of altered mental state with focal neurological signs.



HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient should undergo a computed tomography (CT) scan of his brain to look for pathology such as a space-occupying lesion. Blood tests should be taken to check his lithium level, in addition to tests for other causes of acute confusion, such as hypercalcaemia and abnormal thyroid function. If central nervous system (CNS) infection is suspected, a lumbar puncture should be performed. As the patient has an acute kidney injury, intravenous fluids (0.9% sodium chloride or compound sodium lactate solution) should be commenced. A blood gas should be taken to assess his acid–base status and his fluid balance will need to be clearly monitored.

CASE PROGRESSION

An electrocardiogram (ECG) showed T wave inversion across leads II, III, aVF and V4–6. A CT brain scan was performed and showed no acute changes. Intravenous fluids were commenced and the electrolytes and renal function were monitored daily. A serum lithium level was 2.7 mmol/L (therapeutic range 0.6–1.0 mmol/L).

A magnetic resonance imaging (MRI) scan was difficult to interpret due to movement artefact but appeared grossly normal. Bendroflumethiazide was substituted for 5 mg amlodipine OD.

Final diagnosis: Lithium toxicity.

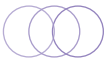
OUTCOME

After 4 days of intravenous fluids, the patient's urea level had normalised and the creatinine had returned to baseline. He was discharged home without further lithium therapy and will be followed up by the community mental health team who are planning to commence olanzapine therapy.

CASE DISCUSSION

Lithium toxicity may develop following overdose or due to changes in renal function. Lithium has a narrow therapeutic window, with a target range of 0.4–1.0 mmol 12 hours post-dose, although individual patients may have specific optimal ranges.

Patients with acute toxicity present with gastrointestinal disturbances, such as nausea and vomiting, while in cases of chronic poisoning, confusion, cerebellar ataxia, drowsiness and seizures may develop. Fine hand tremor is a common side effect of lithium therapy and this may become particularly prominent in lithium toxicity. ECG changes, including first-degree heart block and T wave inversions, may develop in cases of lithium toxicity and can progress to complete heart block.



Management consists of withholding lithium as well as any nephrotoxic drugs and ensuring the patient is adequately hydrated. If significant toxicity is present, haemodialysis is an effective method of eliminating the drug.

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CASE 67: HEPATOMEGALY IN A PATIENT WITH NEWLY DIAGNOSED DIABETES MELLITUS

PATIENT HISTORY

A 46-year-old man presented to the emergency department complaining of intermittent episodes of shortness of breath and palpitations. The episodes started around 4 months earlier but were now becoming more frequent. He denied chest pain and had not identified any exacerbating factors. He had been diagnosed with type 2 diabetes mellitus 2 years ago and had successfully managed this with lifestyle modifications. He took regular gliclazide. He lived with his partner and worked as a labourer on a building site.

EXAMINATION

Initial observations: T 36.8°C, HR 80 bpm, BP 140/90 mm Hg, RR 14, SpO₂ 98% on room air.

The patient was comfortable at rest and looked well. His chest was clear and his heart sounds were normal. His jugular venous pressure (JVP) was not elevated and there was no peripheral oedema. Abdominal examination was significant for hepatomegaly of 2 finger breadths (2.5 cm) below the costal margin.

INITIAL RESULTS

Routine blood tests: WCC 8.8, Hb 152, Plt 317, Na 138, K 4.6, Creat 84, CRP 7.

DIFFERENTIAL DIAGNOSES

The patient has presented complaining of palpitations. Common causes include excess caffeine or alcohol intake, cardiac arrhythmias and hyperthyroidism. He has recently commenced gliclazide and episodes of hypoglycaemia should therefore be considered as a possible cause of palpitations. A pheochromocytoma is a rare cause of palpitations, but this is associated with significant hypertension and diaphoresis.

An infection may be causing intermittent fevers with tachycardia. There is hepatomegaly on examination and infective hepatitis may be a possible diagnosis. Haemochromatosis can lead to symptoms of fatigue and joint pain and both diabetes mellitus and hepatomegaly may develop.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient will need some basic investigations regarding his history of palpitations. A 12-lead electrocardiogram (ECG) may identify an arrhythmia, but if the episodes are infrequent and

of short duration, 24–72 hour ECG recording is more appropriate. A thyrotropin (TSH) level should be measured as thyroid dysfunction is a relatively common cause of tachyarrhythmia. Iron studies (including a ferritin level) should be performed to identify potential haemochromatosis or other iron storage disorders.

Liver enzyme levels (ALT, ALP, AST and GGT) should be added onto the admission bloods and based on these results, a liver ultrasound scan may be arranged. Common autoantibodies to present in primary biliary cirrhosis and autoimmune hepatitis will need to be measured, including anti-mitochondrial, anti-centromere and anti-nuclear antibodies. Hepatitis B, C and HIV serology should also be tested. A thorough alcohol history needs to be taken and if there is any current alcohol misuse then B vitamins should be replaced and a benzodiazepine, such as chlordiazepoxide, should be given if required to manage withdrawal symptoms.

CASE PROGRESSION

An ECG showed normal sinus rhythm and a chest x-ray was normal. Blood tests to investigate for various liver diseases were performed. The patient felt well by the evening and self-discharged before an abdominal ultrasound scan could be performed.

Six months later, he re-presented with an upper gastrointestinal bleed, having ongoing episodes of large volume haematemesis. He was haemodynamically unstable and required a 4-unit packed red cell transfusion prior to an endoscopy. An oesophago-gastro-duodenoscopy (OGD) showed multiple oesophageal varices that required banding.

His blood tests from the initial admission were reviewed and were noted to show high serum iron and ferritin levels. His transferrin saturation percentage level was also markedly elevated. A transcutaneous liver biopsy showed haemosiderin deposition consistent with haemochromatosis.

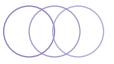
Final diagnosis: Haemochromatosis.

OUTCOME

The patient underwent an echocardiogram, which showed no evidence of abnormal left ventricular function (which can develop in iron overload cardiomyopathy). He commenced a therapeutic venesection programme with phlebotomy sessions occurring based on his ferritin levels. His siblings were screened and were not found to have the common *HFE* gene mutations that cause haemochromatosis. His son is due to undergo screening tests in the coming months.

CASE DISCUSSION

Haemochromatosis develops when mutations in the *HFE* gene lead to iron overload and subsequent organ toxicity. Haemochromatosis is a common autosomal recessive disorder in the Caucasian population. Early symptoms include fatigue, joint pain and non-specific malaise. Over time, patients may develop diabetes mellitus (as in this case), liver disease and



cardiomyopathy. The diagnosis is a challenging one to make and it may take years to identify haemochromatosis in some patients.

Venesection is the mainstay of treatment, although iron chelation with desferrioxamine is required in some cases, particularly where venesection is challenging (e.g. poor venous access or needle phobia) or contraindicated (e.g. hypotension or anaemia). Close relatives of newly diagnosed patients should be screened for asymptomatic disease.

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CASE 68: COLLAPSED FOLLOWING INFLUENZA

PATIENT HISTORY

A 50-year-old woman was brought to the emergency department by her husband, who found her collapsed on the bathroom floor. The patient was awake when he found her and she denied losing consciousness, explaining that she felt light-headed and was unable to sit up. She had been unwell during the preceding 3 days, experiencing fevers, headache and coryzal symptoms, which she had attributed to seasonal influenza. She complained of nausea and muscle aches that had been present for 24 hours. Her past medical history included depression and fibromyalgia. She took regular glucosamine and occasional paracetamol. She worked as a university lecturer and did not drink alcohol or smoke.

EXAMINATION

Initial observations: T 37.9°C, HR 140 bpm, BP 82/50 mm Hg, RR 20, SpO₂ 97% on room air.

The patient appeared pale and shocked. Her airway was patent and her chest was clear. She was cool to touch. It was difficult to comment on her heart sounds due to the tachycardia and a noisy environment in the emergency department. Her abdomen was soft but tender throughout and the patient vomited twice during the assessment. No focal neurological deficits were identified. She attempted to sit up during the examination and had a brief syncopal episode.

INITIAL RESULTS

Routine blood tests: WCC 18.8, N 13.7, L 4.8, Hb 133, Plt 380, Na 126, K 6.4, Creat 96, CRP 66.

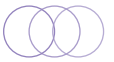
DIFFERENTIAL DIAGNOSES

The patient is haemodynamically unstable with tachycardia and hypotension. She is also febrile with elevated inflammatory markers. She may have a severe viral or bacterial infection causing vasodilatation and cardiovascular compromise. Increased levels of anti-diuretic hormone secretion and subsequent reduced water excretion can lead to the development of hyponatraemia in this context.

Addison's disease (primary adrenal insufficiency) classically presents with fatigue and weakness along with joint pains and muscle aches. An 'Addisonian crisis', where a severe reduction in cortisol leads to cardiovascular collapse, may have developed in this case, possibly due to a recent viral infection or following the physical stress of her fall to the floor prior to admission.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient needs intravenous fluids to be administered immediately – she is dehydrated with circulatory collapse. The fluid of choice in this situation is 0.9% sodium chloride solution.



A urinary catheter should be inserted to monitor her urine output and to guide further fluid replacement. A blood gas should be taken to measure the lactate level (hyperlactataemia is a marker of severe sepsis) and the acid–base status.

Her sodium level should be closely monitored to avoid a rapid increase that could lead to central pontine myelinolysis. Her potassium level is markedly elevated and an ECG should be performed to identify possible T-wave changes. Hyperkalaemia should be managed as per local guidelines and her potassium level should be re-checked in 2–3 hours. A septic screen should be performed and broad-spectrum antibiotics commenced. A serum cortisol level should be taken to detect potential Addison's disease.

CASE PROGRESSION

The patient had a central venous catheter inserted and was transferred to the high dependency unit for aggressive fluid rehydration along with close monitoring of her electrolytes. Intravenous co-amoxiclav and gentamicin were given to treat sepsis of unknown source and intravenous corticosteroids (hydrocortisone) were given to treat a possible Addisonian crisis. A computed tomography (CT) scan of the brain showed no acute pathology.

Twelve hours later, the patient had improved clinically and her blood pressure was stable. Her sodium level had increased to 131 mmol/L. Treatment with intravenous corticosteroids was continued. Viral swabs were positive for H1N1 influenza.

The next morning, her cortisol level was found to be 40 nmol/L (reference range 171–536 nmol/L). An adrenocorticotrophic hormone (ACTH) level was elevated and aldosterone levels were undetectable. A Synacthen (synthetic ACTH) test was performed resulting in a very minor increase in cortisol to 50 nmol/L.

Final diagnosis: Primary adrenal insufficiency presenting with an Addisonian crisis.

OUTCOME

The patient made a rapid recovery over the next 48 hours. She was discharged with hydrocortisone and fludrocortisone therapy. She was given an emergency hydrocortisone injection kit to administer should she become acutely unwell again (while awaiting emergency medical care). Adrenal autoantibodies were detected, consistent with an autoimmune cause of her adrenal insufficiency.

CASE DISCUSSION

Primary adrenal insufficiency (Addison's disease) most commonly develops following autoimmune destruction of the adrenal glands; other causes include adrenal haemorrhage, infarction, malignant infiltration and infections such as HIV and tuberculosis.

Symptoms of primary adrenal insufficiency develop over months to years and are typically non-specific: fatigue, nausea and aches and pains. In this case, it was felt that the patient's pre-existing diagnoses of fibromyalgia and depression may indeed be attributed to her underlying adrenal insufficiency.



An acute crisis may be precipitated following an event such as an infection or trauma, as higher levels of adrenal hormones would usually be produced in response to physical stress. Patients present with postural hypotension, tachycardia, abdominal pain and vomiting.

The condition is diagnosed following an abnormally low level of cortisol, which does not increase following ACTH administration. The normal physiological response to increased ACTH release from the pituitary gland is to upregulate cortisol production by the adrenals. Patients will need replacement of both glucocorticoids (oral hydrocortisone) and mineralocorticoids (oral fludrocortisone).

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CASE 69: ABDOMINAL PAIN AND BLOODY DIARRHOEA

PATIENT HISTORY

A 24-year-old woman presented to the emergency department complaining of an 8-day history of abdominal pain and diarrhoea. She described episodes of central and right upper quadrant abdominal pain that had intensified over the past week and was now 8/10 in severity. The pain was cramping in nature and would often wake her at night. There were no exacerbating or relieving factors. She said that her stool was watery and brown without blood, mucus or visible parasites. She had unintentionally lost 13 kg in weight over the last 6 months. Her past medical history was only significant for a recent gonorrhoea infection and she took no regular medications. She worked as a shop assistant and lived with her friend. She had one regular sexual partner. She was originally from Ethiopia and had moved to the United Kingdom 4 years earlier. She had last travelled abroad 11 months ago when she had visited family in Ethiopia.

EXAMINATION

Initial observations: T 37.6°C, HR 110 bpm, BP 118/80 mm Hg, RR 18, SpO₂ 99% on room air.

The patient appeared alert and generally well. Her chest was clear and the heart sounds were normal. There was generalised abdominal tenderness with voluntary guarding over the right upper quadrant. No lymphadenopathy was present. A digital rectal examination was not performed, but she opened her bowels approximately every 30 minutes during her time in the emergency department and her stool was noted to be Bristol stool chart type 7 (watery) with no blood present.

INITIAL RESULTS

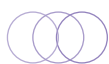
Routine blood tests: WCC 12.4, N 10.5, L 1.1, Hb 110, MCV 77, Plt 172, Na 135, K 4.0, Creat 70, CRP 114, Amylase 110, Bili 12, ALT 38, ALP 50, albumin 37.

DIFFERENTIAL DIAGNOSES

The inflammatory bowel diseases, Crohn's disease and ulcerative colitis, typically present between the ages of 15 and 25 years and symptoms include abdominal pain, weight loss and diarrhoea. Fever and an elevated C-reactive protein (CRP) level may also be present in episodes of severe inflammation.

The patient may have inflammation of the ileum due to infection with *Yersinia enterocolitica* or *Mycobacterium tuberculosis*.

An underlying HIV infection could lead to the development of cytomegalovirus (CMV) colitis or recurrent episodes of gastroenteritis due to immunosuppression. Malignancy, particularly small bowel lymphoma, is another possible cause of the patient's symptoms and signs.



HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

Stool samples should be sent for microscopy and culture plus analysis for ova, cysts and parasites. Stool will also need to be tested for *Clostridium difficile* infection and a faecal calprotectin level (which is elevated in the presence of bowel inflammation) should be sent.

If the patient remains stable, she could be discharged home to await further investigations over the coming days. She will need an abdominal ultrasound scan to look for structural abnormalities. A flexible sigmoidoscopy or colonoscopy can assess for the presence of inflammatory bowel disease.

CASE PROGRESSION

Stool samples were taken. Following 1 L intravenous fluid rehydration, the patient's tachycardia resolved and she was discharged home with an outpatient follow-up clinic booked for the following week. An abdominal ultrasound scan and a flexible sigmoidoscopy were also requested.

The patient re-presented to hospital 24 hours later complaining of worsening abdominal pain. Her temperature was 38.6°C and she now had fresh blood in her stool. Her abdomen remained soft with generalised tenderness. Her stool samples were negative for parasites and bacterial infections including *Escherichia coli*, *Salmonella* spp., *Shigella* spp., *Campylobacter jejuni* and *Clostridium difficile*.

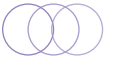
Her CRP level rose to 264 mg/L over the next 48 hours. A flexible sigmoidoscopy showed patchy inflammation in the distal transverse colon, likely to represent Crohn's disease; a biopsy was taken. An abdominal computed tomography (CT) scan showed marked mural thickening of the terminal ileum. There was moderate to large volume ascites and widespread mesenteric fat stranding (representing inflammation) and nodularity. A few prominent para-aortic and pelvic lymph nodes were seen, which were thought to be reactive, in keeping with Crohn's disease.

While the CT scan and the flexible sigmoidoscopy were reported to be consistent with Crohn's disease, the gastroenterology and infectious diseases teams were concerned that tuberculosis was still a possible diagnosis. Induced sputum tests and an ascitic tap were unremarkable. The biopsy from the flexible sigmoidoscopy showed acute and chronic inflammation, including an area of granulomatous inflammation. The Ziehl-Neelsen stain showed a single acid-fast bacillus present, indicative of *Mycobacterium tuberculosis* infection.

Final diagnosis: Gastrointestinal tuberculosis.

OUTCOME

Anti-tuberculosis medications were commenced. The abdominal CT scan was re-reviewed and it was reported that the overall appearances were likely to represent tuberculosis. A CT scan of the chest showed subcarinal and internal mammary adenopathy and prominent superior mediastinal lymphadenopathy, compatible with a diagnosis of tuberculosis.



CASE DISCUSSION

Tuberculosis of the gastrointestinal tract, most commonly around the terminal ileum, can develop following ingestion of infected sputum or via haematogenous or lymphatic spread.

This patient had evidence of abdominal tuberculosis affecting the peritoneum and gastrointestinal tract, but other potential sites of infection include the spleen, adrenal, kidneys, pancreas and liver.

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CASE 70: A PATIENT WITH HIV AND PERSONALITY CHANGE

PATIENT HISTORY

A 40-year-old woman was brought to the emergency department by her husband who reported that her personality had changed dramatically over recent weeks. The patient denied any symptoms and wanted to leave hospital immediately. Her husband explained that she had become paranoid and was refusing to eat as she believed that he had poisoned her food. She complained of frequent headaches and had stopped going to work. She had tested positive for HIV 8 years earlier and had never adhered to anti-retroviral therapy. She took no regular medications. She worked as a traffic warden and had not travelled abroad for 4 years.

EXAMINATION

Initial observations: T 37.3°C, HR 74 bpm, BP 122/86 mm Hg, RR 14 and SpO₂ 99% on room air.

The patient was alert and orientated. Systemic examination, including neurological assessment, was unremarkable. During the examination, the patient told the junior doctor that she was under a voodoo spell, which her husband had performed. She claimed that he had visited a witch doctor and was trying to harm her with magic.

INITIAL RESULTS

Routine blood tests: WCC 14.2, N 12.2, Hb 118, Plt 405, Na 135, K 3.9, Creat 59, CRP 86.

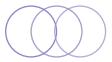
DIFFERENTIAL DIAGNOSES

The patient has a history of being immunosuppressed and diagnoses related to this, such as opportunistic infections, should therefore be considered. Toxoplasmosis typically presents with confusion, drowsiness and personality change preceded by headaches. Single or multiple lesions, which may be ring shaped, are often detectable on computed tomography (CT) imaging, although they are more clearly visualised on magnetic resonance imaging (MRI) scans.

Similarly, tuberculosis meningitis can begin with a worsening headache over a course of days to weeks. Patients will later develop classical symptoms and signs of meningitis, such as photophobia and neck stiffness. Granulomas may be seen on CT or MRI.

Cryptococcal meningitis develops insidiously with headaches, nausea and altered mental state, including personality changes. CT and MRI scans are unremarkable and the fungal infection is usually diagnosed following lumbar puncture.

Progressive multifocal leukoencephalopathy (PML) can occur due to JC virus infection, leading to continuous demyelination within the central nervous system. HIV encephalopathy is a



progressive neurocognitive disorder that has a poor prognosis (several months) without anti-retroviral treatment. Cerebral lymphoma can present with focal neurological signs, headache or altered mental state.

Lastly, the patient may be experiencing a psychotic episode secondary to an underlying mental health condition such as schizophrenia, depression or bipolar affective disorder. Other causes may include thyrotoxicosis, neurosyphilis and exposure to toxins.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

If the patient declines treatment, she should have a formal capacity assessment to establish whether she lacks capacity to make this decision. If she is willing to undergo investigations, blood tests should be sent for the following: corrected calcium, thyrotropin (TSH), vitamin B₁₂ and folate levels, syphilis serology and serum cryptococcal antigen. Her CD4 count and HIV viral load should be measured.

An urgent CT head scan (ideally with contrast), or, if possible, an MRI scan must be requested to identify any pathological lesions and to identify signs of raised intracranial pressure (ICP). Depending on the results of this scan, a lumbar puncture may be considered.

A specialist HIV or infectious diseases team should be contacted to advise regarding further investigations and to consider initiating anti-retroviral therapy.

CASE PROGRESSION

The patient agreed to be admitted for further investigations. A CT head scan, followed by an MRI scan, were both unremarkable. Ceftriaxone and aciclovir were started empirically for possible meningoencephalitis.

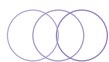
A lumbar puncture was performed, cerebrospinal fluid (CSF) results showed an elevated leucocyte count (80% neutrophils, 20% lymphocytes), an elevated protein level of 0.8 g/L (reference range 0–0.44 g/L) and a reduced glucose level (30% of plasma glucose level). The Gram stain was negative. Of note, the opening pressure was 30 cm H₂O (reference range 10–20 cm H₂O).

The serum cryptococcal antigen was positive. Intravenous amphotericin B and flucytosine were commenced to treat presumed cryptococcal meningitis.

Final diagnosis: Cryptococcal meningitis.

OUTCOME

Within 48 hours, the patient's paranoid symptoms had resolved. She underwent serial lumbar punctures to monitor her ICP with drainage of CSF to maintain a closing pressure of <25 cm H₂O. The patient was discharged with oral fluconazole therapy and was followed up in the outpatient clinic. She returned to work with no further episodes of personality change.



Repeat CSF cultures were negative for cryptococcal antigen. Several weeks later, she commenced anti-retroviral therapy, which had been delayed until this point to minimise the risk of developing immune reconstitution inflammatory syndrome (IRIS), a severe inflammatory response to pre-existing infections that may develop as the immune system recovers.

CASE DISCUSSION

Cryptococcal meningitis typically develops following infection with *Cryptococcus neoformans* in immunocompromised patients. The infection progresses over a course of weeks to months, and patients may present with headache and altered mental status. Acute treatment consists of anti-fungal therapy, which in this case, consisted of amphotericin B and flucytosine initially, followed by oral fluconazole.

Serial lumbar punctures with CSF drainage may be required to reduce ICP.

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CASE 71: PROXIMAL WEAKNESS AND MUSCLE ACHES

PATIENT HISTORY

A 70-year-old man was admitted to the emergency department following an episode of collapse while he was participating in an organised hill walk. He explained that his legs had become progressively weaker during the walk and eventually 'gave way'. He felt that he had become generally weaker over recent weeks, and that, although he maintained an active lifestyle, he had noticed a decline in his exercise tolerance. His past medical history included alopecia areata and psoriasis. He used topical corticosteroid cream several times per week. He lived with his brother and was a retired piano tuner. He was an ex-smoker with a 40 pack year history.

EXAMINATION

Initial observations: T 37°C, HR 90 bpm, BP 138/90 mm Hg, RR 20, SpO₂ 96% on room air.

The patient appeared slightly dyspnoeic but otherwise well. There were violaceous patches of excoriated lesions over his knuckles and elbows (the patient explained that this was psoriasis). His chest was clear to auscultation. Cardiovascular and abdominal examinations were unremarkable. There was marked proximal weakness and the patient complained of myalgia over his shoulders and thighs.

INITIAL RESULTS

Routine blood tests: WCC 13.2, N 10.7, Hb 136, Plt 291, Na 135, K 4.0, Creat 100, CRP 40.

DIFFERENTIAL DIAGNOSES

The patient presents with acute proximal weakness and myalgia on a background of progressive weakness. He has a past history of psoriasis and alopecia, both of which are autoimmune conditions. The patient may have developed an autoimmune inflammatory myopathy, such as dermatomyositis or polymyositis. These conditions present with progressive proximal weakness and in dermatomyositis there is a dusky purple rash over areas including the eyelids, cheeks, torso and extensor surfaces.

Polymyalgia rheumatic is a condition where patients develop pain and stiffness of the muscles of the shoulder and pelvic girdles. There is a strong association with temporal arteritis.

Exercise-induced myalgia (overuse injury) may be causing the patient's symptoms and can lead to rhabdomyolysis. The patient should be specifically asked if he has taken a course of corticosteroids recently, as they can cause a steroid myopathy. Statins are also associated with a drug-induced myopathy.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

Blood samples should be sent for an autoimmune screen to identify conditions such as systemic lupus erythematosus and rheumatoid arthritis (although neither of these conditions commonly present in patients of this age group). Anti-nuclear antibody (ANA), anti-mitochondrial M2 and anti-Jo-1 antibodies are highly associated with autoimmune inflammatory myopathies. A creatine kinase (CK) level should be sent to identify excessive muscle breakdown, due to myositis or rhabdomyolysis. A rheumatology opinion should be sought to guide further investigations.

A magnetic resonance imaging (MRI) scan of the shoulder or pelvic girdle muscles may show peri-muscular oedema and hyperintense signal in inflamed muscles. A muscle biopsy should also be performed where possible.

CASE PROGRESSION

The patient was admitted to hospital for further investigations towards the end of the week. A CK level came back as 18050 U/L (reference range 40–320 U/L). A dermatologist reviewed the lesions on the patient's hands and concluded that they were consistent with Gottron's papules rather than psoriasis.

The patient became increasingly dyspnoeic over the weekend. The rheumatology team reviewed the patient and felt that his symptoms were likely to represent dermatomyositis, possibly with respiratory muscle involvement.

Anti-mitochondrial M2 and anti-Jo-1 antibodies were both strongly positive and a muscle biopsy confirmed that myositis was present.

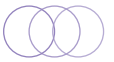
Final diagnosis: Dermatomyositis.

OUTCOME

Intravenous methylprednisolone and cyclophosphamide immunosuppressive therapy was commenced. As the onset of dermatomyositis is often a paraneoplastic phenomenon, a computed tomography (CT) scan of the patient's chest, abdomen and pelvis was carried out to identify possible malignancy. A spiculated mass was noted in the right upper lobe, likely to represent a primary lung cancer.

CASE DISCUSSION

Polymyositis and dermatomyositis are inflammatory myopathies that cause progressive proximal muscle weakness and may involve the oesophagus and respiratory muscles. Dermatomyositis, in particular, is associated with (and may precede) malignancy and patients should therefore be routinely screened for commonly associated malignancies, including lung and breast cancer.



Muscle disease is typically treated with corticosteroids, although additional immunosuppressive agents, such as methotrexate or cyclophosphamide, may be required.

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CASE 72: A RAPIDLY DETERIORATING PATIENT

PATIENT HISTORY

A 24-year-old woman was brought to the emergency department with a 3-month history of worsening epigastric pain. The pain was a dull ache that radiated to the right flank, and was exacerbated by passing urine. She denied any history of fevers or night sweats but did admit to some unintentional weight loss as well as bloating, vomiting and early satiety. On direct questioning, she described intermittent rectal bleeding over the past 4 months. Her past medical history was significant only for asthma. She took the oral contraceptive pill but no other medications. Her family history included first-degree relatives with cancers of the bladder, brain and oesophagus. She worked as a telephone salesperson and neither smoked nor drank alcohol. She had not travelled recently.

EXAMINATION

Initial observations: T 37.2°C, HR 80, BP 118/58, RR 18, SpO₂ 99% on room air.

Systems examination revealed epigastric and left flank pain but no other abnormal findings.

INITIAL RESULTS

Routine blood tests: WCC 10.2, Hb 138, Plt 202, Na 139, K 3.9, Creat 68, CRP 20.

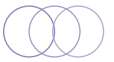
DIFFERENTIAL DIAGNOSES

Inflammatory bowel disease (ulcerative colitis or Crohn's disease) typically presents with cramping abdominal pain associated with diarrhoea, which may contain fresh blood or mucus. Patients usually present between the ages of 15 and 25 years.

A vasculitis, such as polyarteritis nodosa (PAN) may be present. PAN affects small-medium vessels and presents with constitutional symptoms, such as fatigue and general malaise, although abdominal pain and nausea may be present if there is gastrointestinal involvement. Rectal bleeding is an uncommon feature but can occur if an aneurysm or pseudoaneurysm develops within the arteries and arterioles of the gastrointestinal vascular system, or if ischaemic colitis is present.

Gastrointestinal tuberculosis, with lesions in the ileocaecal and colonic regions, may present with rectal bleeding and abdominal pain. Weight loss is commonly associated with tuberculosis infection.

Malignancy, including ovarian and gastric cancer and lymphoma, will also need to be excluded in this patient with weight loss, abdominal pain, rectal bleeding and a strong family history of cancer.



HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

She should be given analgesia to treat her abdominal pain and anti-emetics for her nausea and vomiting. She may need intravenous fluids if she is not tolerating oral intake. A chest x-ray should be performed to look for and mass lesions indicative of tuberculosis or metastases and a plain abdominal x-ray will identify bowel dilatation. She should be reviewed by the surgical team to exclude any surgical cause for her abdominal pain, such as appendicitis.

She should be admitted to an inpatient bed for further investigations, including an autoimmune screen (in view of the possibility of vasculitis) and an ultrasound or computed tomography (CT) scan of her abdomen. A flexible sigmoidoscopy or colonoscopy should also be considered, depending on the results of the above investigations.

CASE PROGRESSION

The patient was admitted under the medical team and was given intravenous fluids and anti-emetics. An abdominal x-ray showed faecal loading and the chest x-ray showed multiple circular lesions in the lungs (Figure 72.1), suspicious for metastases.

A CT scan of the chest, abdomen and pelvis showed a large, retroperitoneal mass around the right adrenal, with metastatic deposits to the lungs, liver and spleen. A multi-organ resection was performed, including a nephrectomy, adrenalectomy and splenectomy. Histology confirmed metastatic adrenal carcinoma. Peritoneal lesions subsequently developed.

Final diagnosis: Metastatic adrenal carcinoma.

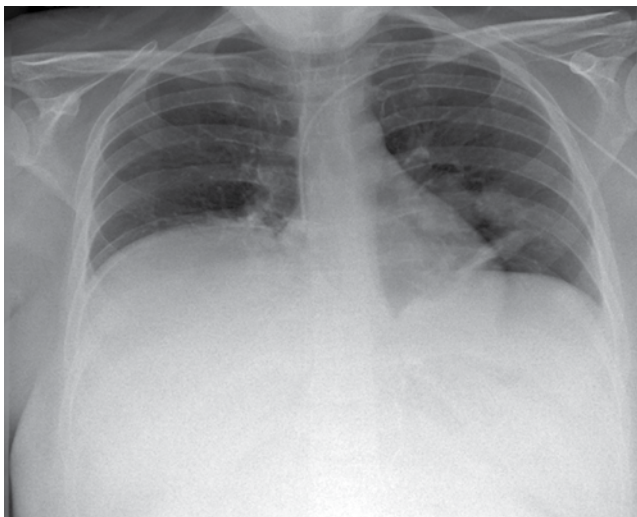
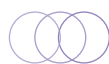


Figure 72.1 Chest x-ray showing multiple circular lesions in the lung fields.



OUTCOME

The patient was transferred to the oncology unit for chemotherapy. She received 4 days of chemotherapy but rapidly deteriorated and was started on end-of-life care.

CASE DISCUSSION

Adrenal carcinoma is a rare cancer that tends to affect both young children and adults in their fourth or fifth decades of life. Typical symptoms include virilisation in children, and Cushing's syndrome (glucocorticoid excess) and/or Conn's syndrome (mineralocorticoid excess). Non-functional tumours may present with abdominal pain and 'red-flag' warning signs, including weight loss. The cancer is highly aggressive, with a 5-year survival rate of 20%–35%. Metastases are often present at the time of diagnosis.

Of note, once an adrenal mass is seen on CT imaging, it should not be biopsied until a pheochromocytoma has been excluded via biochemical testing, as a hypertensive (or hypotensive) crisis may be precipitated.

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CASE 73: PAINLESS JAUNDICE

PATIENT HISTORY

A 55-year-old lady presented to the emergency department complaining of abdominal pain, vomiting and a sore throat. She told of a week-long history of nausea, loss of appetite and intermittent fevers. She stated that her friend had mentioned to her 2 days earlier that she looked 'a bit yellow'. She described pain in the right upper quadrant of her abdomen, which was dull in nature and radiated to her back. Her past medical history was significant for a hysterectomy 5 years earlier due to uterine carcinoma in situ. She was taking tibolone (a synthetic steroid drug with oestrogenic, androgenic and progestogenic properties used as hormone replacement therapy) and calcium carbonate (750 mg) with vitamin D₃ (200 I.U.). She worked at a market stall and reported drinking 5 units of alcohol per week. Within the past fortnight she had ended a long-term relationship with a partner who had an unspecified liver disease and had since had unprotected sexual intercourse with one man, of whom she knew no medical details. She had never injected recreational drugs and had not travelled abroad in recent years.

EXAMINATION

Initial observations: T 36.8°C, HR 80 bpm, BP 134/92 mm Hg, RR 18, SpO₂ 99% on room air.

The patient was visibly jaundiced but otherwise appeared well. Systemic examination was unremarkable, with no palpable organomegaly and no further stigmata of chronic liver disease present.

INITIAL RESULTS

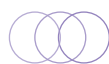
Routine blood tests: WCC 8.8, Hb 147, Plt 369, Na 139, K 3.2, Urea 1.7, Creat 56, Bili 227, ALT 1591, ALP 74, Alb 38, GGT 172, INR 2.07, CRP 3.

DIFFERENTIAL DIAGNOSES

The patient has developed an acute hepatitis. Viral causes of hepatitis include hepatitis B and hepatitis C and HIV, all of which can be sexually transmitted. This patient had a recent relationship with a partner who had liver disease and unprotected sexual intercourse with another partner. Hepatitis E, cytomegalovirus (CMV) and Epstein-Barr virus (EBV) are other potential causes of viral hepatitis in the United Kingdom.

Autoimmune hepatitis can present with signs of either chronic liver disease or acute hepatitis. Females are more commonly affected than males and the majority of patients will complain of constitutional symptoms, including fatigue, fever and weight loss. Other autoimmune hepatobiliary conditions to consider are primary biliary cirrhosis and primary sclerosing cholangitis.

Cholecystitis, biliary sepsis and cholangiocarcinoma are important diagnoses to exclude.



There are isolated case reports of an acute hepatitis developing in patients taking tibolone therapy, but such incidents are rare. Nevertheless, a drug-induced hepatitis should be considered.

Malignancy, particularly in view of the past history of uterine carcinoma, should also be considered.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient should have a liver screen conducted, including viral serology for hepatitis B, C, E, HIV, CMV, and EBV. Serum ferritin levels should be checked to exclude haemochromatosis. An autoimmune screen should be conducted, looking particularly at anti-nuclear antibodies (ANA) and smooth muscle antibodies (SMA), which are associated with autoimmune hepatitis.

An ultrasound scan of the liver should be performed to look for lesions such as metastatic deposits or an abscess and to assess the size of the liver and spleen. A Doppler ultrasound will look at hepatic flow and potentially identify obstruction of hepatic venous outflow resulting in Budd-Chiari syndrome.

The gastroenterology team should assess the patient and consider further investigations at this stage.

CASE PROGRESSION

The patient was admitted under the gastroenterology team for investigation of acute hepatitis. She became pyrexial in the emergency department (T 38°C) and a full septic screen was therefore carried out. In view of her elevated INR, 10 mg vitamin K was administered intravenously, and this continued once daily for 3 days.

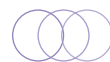
Her ferritin level was elevated at 3528 µg/L (reference range 41–400 µg/L), but the clinical presentation was not consistent with haemochromatosis and the rise was thought to represent an inflammatory response, as ferritin is an acute phase protein.

An ultrasound scan of the liver showed mild intrahepatic duct dilatation. A computed tomography (CT) scan of the abdomen and pelvis, and a triple phase liver CT scan were both unremarkable.

After 1 week in hospital, markers for hepatitis E, CMV, EBV, and alpha 1-antitrypsin disease were within normal range; an autoimmune panel was normal, and tumour markers were not elevated.

A transjugular liver biopsy was carried out, which showed severe interface hepatitis, indicative of autoimmune hepatitis.

Final diagnosis: Seronegative autoimmune hepatitis.



OUTCOME

Immunosuppressive treatment with intravenous methylprednisolone and azathioprine was commenced, but the patient responded poorly. She was transferred to a tertiary hepatology centre to await a liver transplant.

CASE DISCUSSION

In this case, lactulose was commenced at the beginning of the admission and the aim was for the patient to have three to four loose bowel motions per day. Lactulose reduces ammonia levels, which can accumulate and lead to hepatic encephalopathy. Lactulose works via two actions: (1) by reducing bowel transit time and therefore the time available for protein to be metabolised to ammonia, and (2) by reducing the bowel pH and thus promoting conversion of ammonia to ammonium ions. When intravenous fluids were given to the patient, 5% dextrose solution was chosen, as there can be marked impairment of gluconeogenesis in hepatic failure.

Seronegative autoimmune hepatitis is a relatively common cause of acute hepatitis leading to end-stage liver failure requiring transplantation. The majority of patients, however, will achieve disease remission following treatment with corticosteroids and azathioprine.

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CASE 74: A BLISTERING RASH

PATIENT HISTORY

A 46-year-old woman presented to the emergency department complaining of a painful rash. She gave a history of noticing what she described as 'red spots' on her right leg 3 weeks earlier. Two days ago, the rash had spread to cover most of the back of her leg. The underlying skin now felt hot and pruritic and she also reported experiencing myalgia and lethargy. Her past history included a stroke 2 years earlier and subsequent epilepsy. Her regular medications included furosemide, clopidogrel, folic acid and sodium valproate. She was allergic to penicillins. She worked from home as an online retail assistant and lived with her friend. All close contacts were well. She had never smoked and drank minimal alcohol. She had no travel history.

EXAMINATION

Initial observations: T 37°C, HR 78 bpm, BP 136/82 mm Hg, RR 14, SpO₂ 99% on room air.

The patient appeared clinically well. There were several tense blisters over the flexor surface of her right leg, with areas over the calf where blisters had burst leaving multiple erosions (see [Figure 74.1](#)). Her chest was clear to auscultation and her heart sounds were normal. Her jugular venous pressure (JVP) was elevated and she had bilateral pitting oedema to mid shin, which was reported to be longstanding.

INITIAL RESULTS

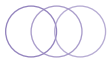
Routine blood tests: WCC 5.0, Hb 15.0, Plt 138, Na 142, K 3.5, Urea 4.1, Creat 60, CRP 50.

DIFFERENTIAL DIAGNOSES

The patient presents with a 3-week history of a blistering rash on a background of a previous stroke and possible heart failure.



Figure 74.1 Erosions over the patient's skin where blisters have ruptured.



Bullous impetigo, usually caused by *Staphylococcus aureus*, is a fairly common infectious skin condition. Infections are more common in children, immunosuppressed people and those who work in institutions such as hospitals or schools.

Immunobullous conditions, including pemphigoid and pemphigus, present in older adults and are differentiated by the quality of the bullae – tense bullae form in pemphigoid whereas flaccid bullae that rupture easily are present in pemphigus.

Contact dermatitis can present with blistering lesions. The patient should be asked whether she has been exposed to any new detergents, fabric conditioners or lotions over the days preceding the development of the rash.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The eroded lesions where blisters have burst should be swabbed and sent for bacterial culture. A full autoimmune screen should be sent and a dermatology opinion should be sought. If there are concerns about possible localised infection, oral antibiotics should be commenced.

CASE PROGRESSION

The patient was admitted under the medical team for further investigation of her lesions. Clarithromycin was commenced for possible cellulitis and, although this diagnosis was excluded within hours, the decision was made to continue the antibiotic in case of bacterial infection within the eroded lesions.

Over the next 24 hours, she developed bullae over her left leg and right arm. The dermatology team reviewed the patient and felt that the main differential diagnoses were pemphigoid, pemphigus and a viral blistering rash.

The dermatologists took a focussed history, eliciting that the patient had a history of multiple miscarriages and noting that she was of a young age to experience a stroke. They described observing tense blisters that were pale yellow on an erythematous background. They also noted the non-blanching rash covering the arms. There was no oral involvement. A skin biopsy was taken.

The dermatology team diagnosed bullous pemphigoid with a probable background of antiphospholipid syndrome and treated the patient with topical steroids (mometasone) and a lotion containing liquid paraffin, isopropyl myristate, benzalkonium chloride and chlorhexidine hydrochloride.

Final diagnosis: Bullous pemphigoid.

OUTCOME

Bullous pemphigoid was confirmed with direct immunofluorescence. The lupus and antiphospholipid screens were negative. The patient's rash gradually resolved over the following days and she was discharged home, to be followed up in the dermatology clinic. The lupus



anti-coagulant test was positive on this admission and she is awaiting a repeat test once she has recovered from this acute illness.

CASE DISCUSSION

Bullous pemphigoid is more common and typically far less aggressive than pemphigus vulgaris. It is an autoimmune condition whereby autoantibodies attack the hemidesmosomes and thus disrupt the basement membrane of the epidermis, resulting in tense blistering lesions.

Interestingly, bullous pemphigoid is associated with a past history of anti-phospholipid syndrome and anti-phospholipid antibodies are commonly detected in patients with autoimmune bullous diseases. The dermatology team suspects that the patient will eventually be diagnosed with anti-phospholipid disease.

Drugs are another possible precipitant for the development of bullous conditions, with furosemide, which this patient was taking daily, being the most commonly reported medication to induce pemphigoid.

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CASE 75: A PATIENT WITH CROHN'S DISEASE AND WORSENING DIARRHOEA

PATIENT HISTORY

A 53-year-old lady presented with a 5-day history of diarrhoea and vomiting. She had known Crohn's disease, which was normally well controlled. She was seen in the emergency department and diagnosed with a flare of Crohn's disease. Her observations were stable and she appeared clinically well. She was discharged with a course of oral prednisolone and advised to attend the gastroenterology outpatient clinic. She returned to the emergency department 4 days later, complaining that she was opening her bowels 10 times daily, passing loose, yellow motions with associated abdominal pain. Her past history also included rheumatoid arthritis, atrial fibrillation and hypertension. She was unsure which medications she was taking, aside from methotrexate. She worked as a catering assistant and did not smoke or drink alcohol.

EXAMINATION

Initial observations: T 36.5°C, HR 60, BP 96/70, RR 20, SpO₂ 96% on room air.

The patient appeared to be in discomfort and was grimacing with pain. Cardiovascular and respiratory examinations were unremarkable. Abdominal examination identified diffuse lower abdominal pain with rebound tenderness.

INITIAL RESULTS

Routine blood tests (visit 1): WCC 8.3, Hb 125, Plt 179, Na 135, K 4.0, Creat 67, CRP 71.

Routine blood tests (visit 2): WCC 22.6, Hb 172, Plt 400, Na 126, K haemolysed, Creat 149, CRP 71.

DIFFERENTIAL DIAGNOSES

The patient presents with abdominal pain and diarrhoea. Between her two visits to the emergency department, her renal function has deteriorated significantly. The most probable explanation is that she is experiencing a severe flare of her Crohn's disease. This could be due to missed medications (the patient was unsure of her drug history), a recent infection or any physical or emotional stress.

The patient may have gastroenteritis, with common bacterial infections including *Campylobacter jejuni*, *Clostridium perfringens*, *Escherichia coli*, *Salmonella* spp. and *Shigella* spp.

Thromboembolism leading to occlusive ischaemia of the gastrointestinal arterial circulation can result in mesenteric ischaemia or ischaemic colitis. This patient has a past history of atrial fibrillation so is at increased risk of thromboembolic disease. Although she was unable

to recall her drug history, she should be specifically asked whether she is taking an anti-coagulant medication. Her INR should be tested – this will be elevated if the patient is taking warfarin.

An Addisonian crisis should also be considered as this is a medical emergency. Patients present with hypotension and abdominal pain; bloods typically show hyponatraemia, hyperkalaemia and elevated creatinine levels. She was prescribed corticosteroids 4 days earlier – it would be useful to establish whether she is taking a long-term course of steroids and whether her symptoms may be due to glucocorticoid deficiency from taking a lower dose of prednisolone.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

Intravenous fluids should be commenced and the patient kept ‘nil-by-mouth’ in case surgery is required. A blood gas should be taken to measure the lactate level, which is a measure of anaerobic metabolism and is positively correlated with mortality. The blood gas should also show a potassium level, which will guide fluid replacement. Depending on the potassium level, it would be appropriate to give either 0.9% sodium chloride or compound sodium lactate (Hartmann’s solution) in 500 mL aliquots and re-evaluate the patient’s fluid status frequently.

An abdominal x-ray will need to be performed to assess for dilated loops of bowel and to rapidly identify toxic megacolon. The surgical team should review the patient and advise further management if they believe that the patient has an acute abdomen. A computed tomography (CT) scan of the abdomen is likely to be required.

Stool should be sent for bacterial culture and, if there is concern that there is sepsis, you should consider starting broad-spectrum antibiotics, including cover for *Campylobacter jejuni* if she is immunosuppressed. A random cortisol level should be checked if an Addisonian crisis is suspected.

CASE PROGRESSION

The patient was reviewed by the surgical registrar who reported that she had a tender abdomen with voluntary guarding, but this was not felt to represent an acute abdomen. The registrar requested a magnetic resonance imaging (MRI) scan of the abdomen focusing on the small bowel. They also advised that the gastroenterology team take over further care of the patient.

Intravenous hydrocortisone was commenced (replacing oral prednisolone) to treat a probable Crohn’s flare-up and to prevent symptoms of corticosteroid withdrawal. The gastroenterology team reviewed the patient and decided that the optimal radiological test in this case would be a CT scan of the abdomen.

Despite aggressive fluid rehydration, the patient remained oligouric and hypotensive. She developed shortness of breath and a subsequent examination showed signs of pulmonary oedema – compare admission chest x-ray ([Figure 75.1](#), left chest x-ray) with a repeat film 24 hours later ([Figure 75.1](#), right chest x-ray). She was admitted to the high dependency unit where a central venous catheter was sited and her fluid balance was closely monitored.

The CT showed a large volume of free fluid and bowel wall oedema in keeping with a diffuse colitis (see [Figure 75.2](#)). A flexible sigmoidoscopy was subsequently performed, showing

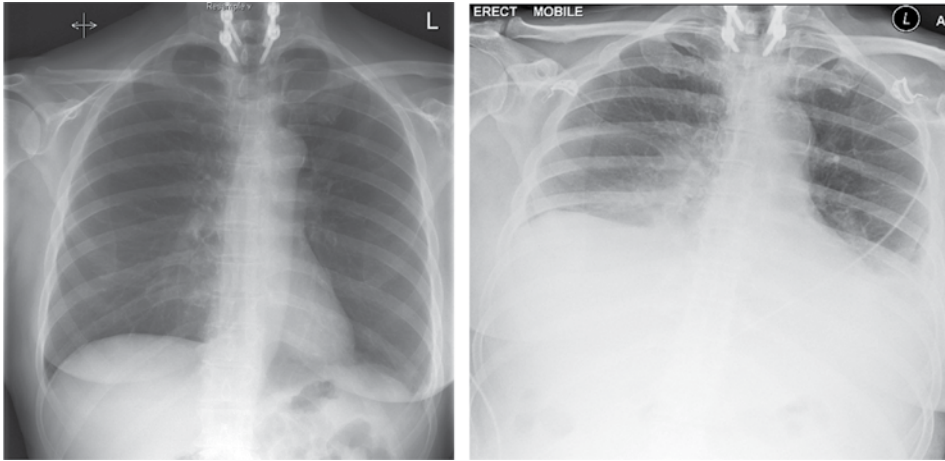
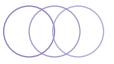


Figure 75.1 Chest x-rays taken at admission (left; normal) and 24 hours later (right; pulmonary oedema).

severe pseudomembranous colitis (see pseudomembranes in [Figure 75.3](#)). Stool samples confirmed *Clostridium difficile* infection. Her white blood cell count rose to $34 \times 10^9/L$. Vancomycin was commenced to treat the infection.

Final diagnosis: *Clostridium difficile* infection.

OUTCOME

The patient deteriorated further, developing severe sepsis. She was transferred to the intensive treatment unit and on her third day of admission, the surgeons performed a subtotal colectomy.

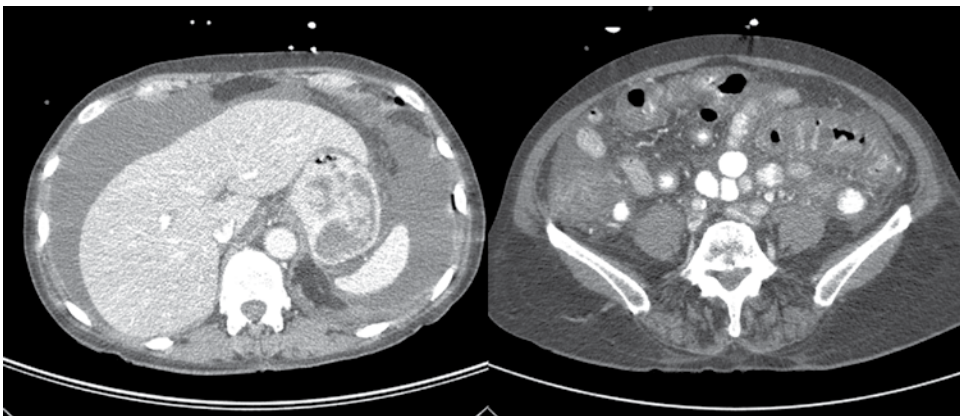


Figure 75.2 CT abdomen scan showing a large volume of free fluid and bowel wall oedema.

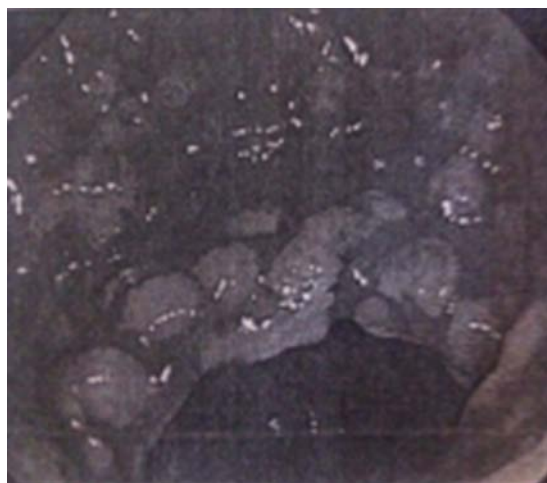


Figure 75.3 Sigmoidoscopy views with pseudomembranes present.

The pharmacist obtained a copy of her recent prescriptions from her general practitioner. She had been on multiple courses of antibiotics, including clindamycin, for 3 months for an infected ulcer on her toe.

She made a gradual recovery over the next 3 weeks and was discharged home.

CASE DISCUSSION

Clostridium difficile infection is more common in patients with immunosuppression (the patient was taking methotrexate and corticosteroids in this case) and prolonged courses of antibiotics. The bacteria are transmitted via the faecal–oral route and a symptomatic infection begins as the *Clostridium difficile* replace the normal gut flora, which may be depleted following antibiotic therapy. Vomiting is unusual, but diarrhoea is common and an antibiotic history should be taken for all those presenting with diarrhoea.

Of note, the patient's white blood cell count was markedly elevated when she re-presented to hospital. Leucocytosis can develop with steroid use but is also frequently a feature of *Clostridium difficile* infection, where the cell count can reach $60\text{--}70 \times 10^9/\text{L}$.

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CASE 76: A SILENT PATIENT

PATIENT HISTORY

A man in his 30s was found collapsed in a thorn bush by a passer-by. He was wearing only trousers with bare feet and appeared unkempt. He did not respond to verbal communication and remained silent during the assessment. He had no possessions with him to provide clues as to his identity.

EXAMINATION

Initial observations: T 38.5°C, HR 140 bpm, BP 136/78 mm Hg, RR 20, SpO₂ 99% on room air.

The patient's Glasgow Coma Scale (GCS) score was 8/15 (E1, V2, M5). His chest was clear and heart sounds were normal with no audible murmurs. His abdomen was soft with no palpable organomegaly. There were no stigmata of chronic liver disease present. Neurological examination identified increased tone in all four limbs, with the upper limbs affected more than the lower limbs. The reflexes were brisk, but there was no clonus present and plantars were down going. The patient's eyes were rolled back for much of the examination, but pupils were documented as equal and of normal size. He was grinding his jaw and making occasional jerking movements as though experiencing muscle spasms (possibly myoclonus). There was no tongue biting or incontinence and he did not appear to have sustained any trauma or assault. He was of Afro-Caribbean origin, had good dental hygiene, had no signs of intravenous drug use and he did not smell of alcohol.

INITIAL RESULTS

Routine blood tests: WCC 8.3, N^o5.3, L^o 2.2, Hb 150, Plt 215, Na 142, K 4.6, Creat 107, CRP 4 and CK 361.

Electrocardiogram (ECG): Sinus tachycardia with a normal QTc interval.

DIFFERENTIAL DIAGNOSES

Meningoencephalitis should be strongly suspected in this patient with fever, tachycardia and altered mental state. This could be a viral or bacterial infection and he should be treated empirically for both.

The patient may be reacting to recreational drugs with stimulant properties. Alternatively, if he has recently commenced anti-psychotic medication, such as olanzapine, quetiapine, amisulpride or risperidone, he may have developed neuroleptic malignant syndrome due to dopamine D₂ receptor blockade. This can result in fever and tachycardia, due to hypothalamic involvement, altered mental consciousness and muscle rigidity. Patients usually have a grossly elevated creatine kinase (CK) level due to muscle rigidity.

Serotonin syndrome may develop following therapeutic use, recreational use or overdose of drugs, which cause increased serotonergic activity. Symptoms include an altered mental state, hyperthermia, tachycardia and myoclonus.



Status epilepticus may present with sustained tonic–clonic or complex partial seizures. The jerking movements and jaw grinding may represent epileptic activity.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

A computed tomography (CT) scan of the patient's brain should be performed to identify pathology such as a subarachnoid haemorrhage, an intracerebral bleed or a space-occupying lesion. An antibiotic and an antiviral agent (typically ceftriaxone and aciclovir) should be commenced to treat meningoencephalitis and a lumbar puncture should be performed, providing the CT head scan shows no signs of raised intracranial pressure (ICP) and the patient has normal coagulation and clotting function.

He may be suffering from sepsis from another source and should be thoroughly examined from top to toe to look for localised signs of infection. Intravenous paracetamol should be given and the patient should be cooled by removing bed sheets.

The police should be contacted to inform them that the patient may be a missing person.

CASE PROGRESSION

The patient was felt to be at risk of airway compromise and was therefore intubated. A CT head scan showed no abnormalities and a lumbar puncture was unremarkable. Intravenous ceftriaxone and aciclovir were commenced. The patient was transferred to the intensive treatment unit. The following morning, his blood results showed a rise in CK (2914 units/L) and his urine was brown, consistent with rhabdomyolysis. He was extubated and intermittently obeyed commands. There was still increased tone, brisk reflexes and down-going plantars. He displayed trismus with facial twitching and actively resisted eye opening.

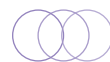
A toxicology screen was negative for 3,4-methylenedioxymethamphetamine (MDMA) and amphetamine use. He was reviewed by the toxicology, neurology and infectious diseases teams. The impression was of an acute dystonia, so a trial of procyclidine was given, with no improvement. Bromocriptine was commenced for possible neuroleptic malignant syndrome.

A phone call was received from a local psychiatry hospital describing a missing person that fitted with this patient. He had known paranoid schizophrenia with similar presentations in the past following prolonged non-compliance with antipsychotic medications. He had previously been diagnosed with malignant catatonia. On this occasion, he had missed several doses of his monthly flupentixol injections.

Final diagnosis: Malignant catatonia.

OUTCOME

Following reintroduction of antipsychotic medications, the patient made a good recovery and was due to be discharged home. Unfortunately, he absconded and was returned to hospital by the police. His mental state deteriorated. He was detained under Section 2 of the Mental Health Act and transferred to an inpatient psychiatric bed.



CASE DISCUSSION

Catatonia can present in a variety of ways, including stupor, maintenance of a rigid pose and repetitive movements. The condition can develop in relation to psychiatric conditions, such as schizophrenia, depression and bipolar affective disorder, as well as medical problems (neurological, e.g. encephalitis) and in the context of toxin administration. Management is usually based on treating the underlying cause, and introducing benzodiazepine therapy. Patients with catatonia typically respond rapidly to intravenous benzodiazepines, such as lorazepam.

Central dopaminergic hypoactivity can lead to malignant catatonia, which has a high mortality rate. Signs include fever and autonomic dysfunction and patients deteriorate rapidly over a period of days. Patients should be managed in a high dependency or intensive treatment unit where they can receive autonomic support and receive active cooling therapies. Benzodiazepines form the mainstay of acute pharmacological treatment, but electroconvulsive therapy is often required for severe cases.

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CASE 77: HIV AND SEIZURES

PATIENT HISTORY

A 35-year-old woman was brought to hospital by ambulance following a witnessed tonic-clonic seizure. She had been walking with a friend and had apparently become confused and disorientated, speaking nonsensical statements, prior to collapsing and having a seizure. There was no tongue biting or incontinence. Her Glasgow Coma Scale (GCS) score was 11/15 when she first arrived to the emergency department. She had a further tonic-clonic seizure shortly after her arrival, which terminated following administration of diazepam. Her friend said that she had no known past medical or drug history. She worked as a care assistant and was originally from Sierra Leone origin. She lived with her two school-aged children. No further history was available.

EXAMINATION

Initial observations: T 37°C, HR 102, BP 174/137 mm Hg, RR 18, SpO₂ 94% on room air.

At the time of examination, systems examination was unremarkable, aside from a GCS of 14 (E4, M6 and V4). Plantars were down going.

INITIAL RESULTS

Routine blood tests: WCC 2.9 (N° 1.4, L° 1.1), Hb 94, PLT 200, Na 134, K 4.0, Creat 122, CRP 1.

Urine dip: +1 protein, +1 blood and negative β-HCG.

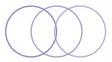
DIFFERENTIAL DIAGNOSES

The patient may have experienced a seizure secondary to epilepsy. This could be longstanding or she may have developed this more recently. In the vast majority of cases, idiopathic generalised epilepsy presents within the first two decades of life, although it may develop throughout adulthood.

Other common causes of seizures include electrolyte abnormalities, hypoglycaemia and alcohol withdrawal. The patient may have suffered from a subarachnoid haemorrhage or an intracranial bleed. Space-occupying lesions, including primary and secondary malignancies, may also present with seizures.

If the patient has underlying HIV, she will be at risk of opportunistic infections, including toxoplasmosis and tuberculosis, both of which can present with cerebral lesions. Cerebral lymphoma is another possible cause of new-onset seizures.

The patient has a markedly elevated blood pressure and thus hypertensive encephalopathy should form part of the differential diagnosis, although hypertension is not uncommon during a seizure or in the immediate post-ictal period.



HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

An anti-epileptic agent should be commenced, as per local guidelines, to prevent ongoing seizure activity. A computed tomography (CT) scan of the brain should be performed, looking for a space-occupying lesion or a haemorrhage. Blood tests should be sent, including glucose, magnesium, phosphate and calcium levels, as well as an HIV test. Once the patient is more alert, she should be re-clerked to establish her medical history.

CASE PROGRESSION

A CT scan showed heterogenous lesions in the left temporal, parietal and occipital lobes with mass effect and midline shift (see [Figure 77.1](#)). The neurosurgical team advised starting intravenous 4 mg dexamethasone BD to reduce the vasogenic oedema and recommended that an urgent magnetic resonance imaging (MRI) scan be performed. Phenytoin was commenced to prevent further seizures.

The MRI scan showed several enhancing lesions in the occipital lobes bilaterally and the left temporal lobe (see [Figure 77.2](#)), some of which were ring shaped. In view of the ring-enhancing lesions, the differential diagnosis now included: primary brain tumours (glioblastoma), cerebral metastases (e.g. primary breast cancer), bacterial abscesses, toxoplasmosis, lymphoma, tuberculomas and neurocysticercosis.

A CT chest/abdomen/pelvis scan showed no abnormalities. The oncology team reviewed the case and arranged a review at the neuro-oncology multidisciplinary meeting as a case of presumed intracerebral metastases with an unknown primary malignancy.

Following this, the patient's HIV test came back positive with a CD4 count of 11 (reference range 450–1660 cells/mm³) and a viral load of 140,000 copies/mL. Following



Figure 77.1 CT brain scan showing lesions in the left temporal, parietal and occipital lobes with midline shift present.

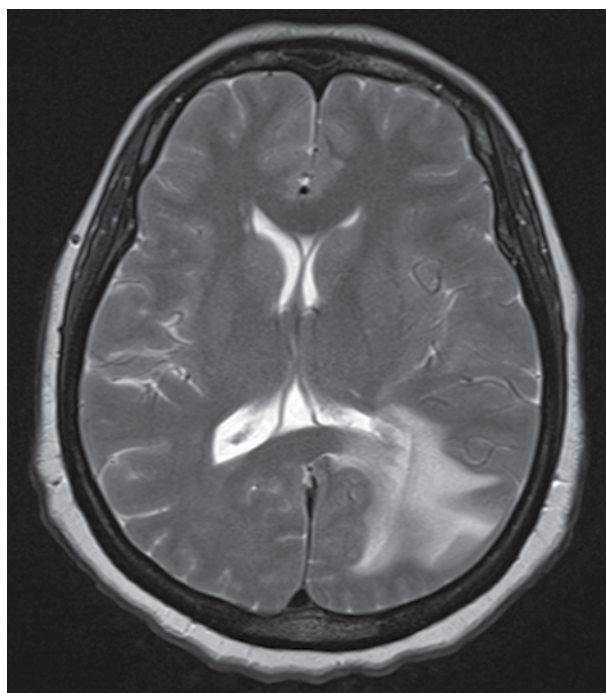


Figure 77.2 MRI brain scan – enhancing lesions within the occipital lobes bilaterally and the left temporal lobe.

serological testing, a diagnosis of cerebral toxoplasmosis, rather than brain metastases, was made. Pyrimethamine and clindamycin were commenced by the specialist HIV team. The neurology team prescribed regular levetiracetam in place of phenytoin.

Final diagnosis: Cerebral toxoplasmosis secondary to immunosuppression.

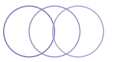
OUTCOME

The patient has had difficulties accepting her diagnosis and is reluctant to continue anti-retroviral therapy. She is receiving ongoing support from the specialist HIV team. Her impaired renal function was investigated and was found to be secondary to HIV-associated nephropathy. Her children both tested negative for HIV infection.

CASE DISCUSSION

Toxoplasmosis can be acquired through eating undercooked meat, consuming substances contaminated with cat faeces or congenitally. It is estimated that over 90% of Europeans have been exposed to toxoplasmosis and are IgG seropositive. Following initial exposure, people can develop rashes and non-specific malaise but many are asymptomatic.

In immunocompromised people the toxoplasmosis infection can reactivate. Manifestations include chorioretinitis, encephalitis, brain abscesses, myocarditis and pneumonitis. Acute



toxoplasmosis is treated with pyrimethamine plus clindamycin or sulfadiazine. Folinic acid supplementation prevents sulfadiazine-induced bone marrow suppression.

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CASE 78: DYSARTHRIC, DYSPHAGIC AND POLYURIC

PATIENT HISTORY

A 49-year-old man was referred from the local psychiatric unit with a deteriorating Glasgow Coma Scale (GCS). He had been admitted to the unit 4 weeks earlier after neighbours reported that he appeared unkempt and disorientated. Since admission, the psychiatry team noted that the patient had become increasingly dysarthric, dysphagic, polyuric with urinary incontinence and agitated with new visual hallucinations. He complained of cough, weight loss and profound polydipsia. His past history included bipolar affective disorder, for which he took regular aripiprazole, diazepam and sodium valproate. Until several days earlier, he had been on lithium, quetiapine and procyclidine. He lived alone and was previously independent, smoked 12.5 g tobacco daily and did not drink alcohol.

EXAMINATION

Initial observations: T 37.4°C, HR 80 bpm, BP 130/94 mm Hg, RR 28, SpO₂ 98% on room air.

The patient's GCS score was 12/15 (E4, V2, M6) but systems examination was otherwise unremarkable (he did not comply with a neurological examination).

INITIAL RESULTS

Routine blood tests: WCC 7.4, Hb 128, PLT 212, Na 157, K 4.5, urea 15.1, creat 191 and CRP 54.

DIFFERENTIAL DIAGNOSES

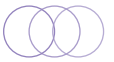
Meningoencephalitis should be suspected in this patient with focal neurology, altered mental state and a low-grade fever. Possible causes of meningoencephalitis are bacterial (including tuberculosis and syphilis), viral (commonly herpes simplex virus [HSV]), and parasitic (toxoplasmosis) infections. Autoimmune and limbic encephalitis are additional possibilities.

Valproate-induced hyperammonaemic encephalopathy, although rare, should be considered. Patients present with an altered mental state and focal neurological deficits.

The patient's symptoms could represent progression of his psychiatric disorder and he requires an urgent neurological examination to determine whether focal neurological signs are present.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient has an acute kidney injury and is hypernatraemic. The choice of intravenous fluids should be guided by both the sodium level and the relative water deficit. As a general rule, when treating hypo- and hypernatraemia in a ward-based setting, you should aim to correct



sodium levels by no more than 8–12 mmol/L per 24 hours. This patient will need strict monitoring of his fluid input and output alongside regular electrolyte measurements, ideally in a high dependency unit setting. A urinary sodium level and paired urine and serum osmolalities should be sent.

A chest x-ray should be performed, given the patient's history of cough, low-grade fever and elevated C-reactive protein (CRP) level. A urine dip should also be performed, looking for the presence of leucocytes or nitrite, which may indicate that a urinary tract infection is present.

A computed tomography (CT) head scan should be performed to identify possible intracerebral causes of his symptoms, although he is unlikely to comply with this investigation. With patients who lack capacity to make decisions regarding their care, treatment should be initiated with careful consideration, but as soon as possible. Sedation and even intubation may be required to achieve emergency care.

Depending on the above results, a lumbar puncture may be required to investigate possible infectious cases of his symptoms.

CASE PROGRESSION

Intravenous fluid rehydration was attempted, initially with 5% dextrose solution, followed by compound sodium lactate (Hartmann's solution), but the patient removed his cannula every time one was inserted. For 2 days, he received <1 L fluid daily due to lack of adherence. He did tolerate a CT head scan, which showed no abnormality. A magnetic resonance imaging (MRI) scan was attempted, but the patient did not tolerate this.

Over several days, his sodium level continued to rise, reaching a peak of 180 mmol/L. His renal function deteriorated significantly. At this stage, he was sedated and intubated and transferred to intensive care unit for further management.

Intravenous (IV) fluid rehydration was carried out and the sodium level normalised. The polyuria progressed and a diagnosis of nephrogenic diabetes insipidus secondary to lithium use was made. Desmopressin was commenced. An MRI showed evidence of mild central pontine myelinolysis (see [Figure 78.1](#)).

Final diagnosis: Central pontine myelinolysis and metabolic brain injury secondary to rapid sodium shifts; underlying sodium imbalance due to lithium-related nephrogenic diabetes insipidus.

OUTCOME

Following intensive physiotherapy and occupational therapy, the patient gradually improved and was discharged home, although a degree of cognitive impairment persisted.

CASE DISCUSSION

Extracellular fluid osmolality is primarily determined by the sodium level. A hypernatraemic state represents a net deficit of water relative to sodium. Rapid changes in sodium levels

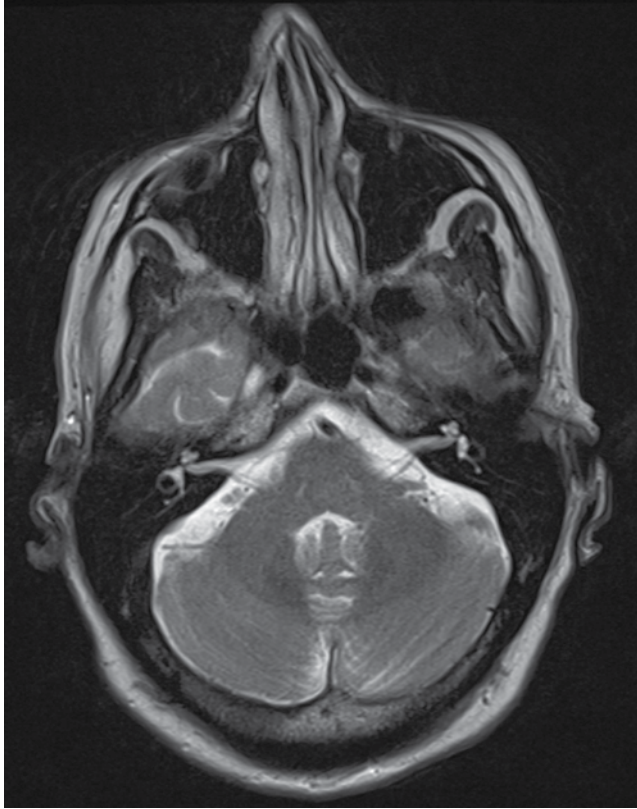


Figure 78.1 MRI brain scan with high signal consistent with central pontine myelinolysis.

can lead to oedema formation, destroying the myelin sheath around neurons and causing an osmotic demyelination brain injury, as occurred in this case. Sudden shifts in osmotic pressure can also lead to cerebral haemorrhage.

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CASE 79: A RELENTLESS RASH

PATIENT HISTORY

A 35-year-old man was admitted from the emergency department with a 48-hour history of a rash over his face and trunk, in addition to fevers and diarrhoea. Four weeks earlier, he had been diagnosed with HIV during a routine sexual health screen and had commenced co-trimoxazole for *Pneumocystis jirovecii* pneumonia (PCP) prophylaxis. At that time, the p24 antigen test was negative, indicating that HIV seroconversion had not occurred within recent weeks. He subsequently attended the emergency department 2 weeks later, where he complained of fevers and malaise. His urine dip had been positive for leucocytes and he commenced a 7-day course of oral co-amoxiclav for a presumed urinary tract infection (urine culture later showed no growth). His general practitioner had also prescribed a course of flucloxacillin when the rash had first developed 2 days earlier. He had no other past medical history and took no other medications. He worked as a pharmacist and lived with his partner. He had travelled to Florida in the past 2 months, did not drink alcohol and had never smoked.

EXAMINATION

Initial observations: T42°C, HR 128 bpm, BP 94/44 mm Hg, RR 20, SpO₂ 95% on room air.

There was a florid, violaceous, maculopapular rash covering the patient's body (see [Figure 79.1](#)). There was no palpable lymphadenopathy and no mucosal lesions. The rest of the examination was unremarkable.

INITIAL RESULTS

Routine blood tests: WCC 7.6, Hb 139, PLT 216, Na 126, K 3.8, Creat 85, CRP 88.

DIFFERENTIAL DIAGNOSES

The patient is febrile, hypotensive and tachycardic with a widespread rash. Measles is a highly infectious viral illness, which presents with fever and a rash that is in keeping with the above description. Has this patient received childhood measles immunisations (in which case the diagnosis would be less likely)? The rash could represent a viral exanthem in the context of other acute infections, such as rubella or viral hepatitis.

Bacterial infections may also present with a widespread exanthema, including staphylococcal and streptococcal toxin infections. *Mycoplasma pneumonia* can develop insidiously over a number of weeks and patients may have a prominent rash, which is in keeping with this patient's history and the fact that he has reduced oxygen saturations. Bacterial meningitis is one of the most important diagnoses to exclude as this can progress rapidly and has a high mortality rate.

Lastly, the patient could be experiencing a drug reaction, possibly in response to one of the recent doses of antibiotics. Does the patient have a previous history of penicillin allergy?



Figure 79.1 Photograph showing the patient's rash at presentation.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient should have a full septic screen, including blood cultures and a chest x-ray. He should be given intravenous fluids, such as compound sodium lactate (Hartmann's solution). Intravenous paracetamol should also be given to reduce his fever. He may require cooled intravenous fluids and other active cooling measures.

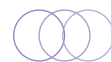
An arterial blood gas should be performed to assess his oxygenation, his acid–base status and the lactate level. Broad-spectrum anti-biotics should be commenced to treat possible bacterial sepsis, although drugs of the penicillin class should be avoided unless there is a clear history that he is not allergic to them.

If measles is suspected, the patient will need to be barrier nursed in a side room. If he does not respond to initial treatment in the emergency department, he may require admission to the high dependency unit for closer monitoring.

CASE PROGRESSION

The patient confirmed with the medical team that he had several courses of beta-lactam antibiotics in his teenage years without incident. He was thus commenced on intravenous co-amoxiclav and gentamicin to treat bacterial sepsis of unknown source. Intravenous fluids were given and his blood pressure improved, although he remained febrile and tachycardic. A blood film showed a relative eosinophilia, although his eosinophil count had not been elevated when his full blood count was checked.

The infectious diseases team was concerned that the patient may have a measles infection. They noted the presence of buccal lesions and advised stopping co-amoxiclav in case this was the cause of a drug reaction (he had been taking this orally prior to admission). The dermatology



team saw the patient and thought the rash represented a viral exanthem. They performed a skin biopsy and planned to review the patient in 2 days' time with the result of this.

The patient became increasingly tachycardic (HR 160) with hypotension (SBP 80 mm Hg) and was transferred to the intensive treatment unit for ongoing care. He received aggressive intravenous fluid hydration and he became haemodynamically stable over the next 24 hours. The dermatology team saw the patient and diagnosed likely DRESS syndrome (drug reaction with eosinophilia and systemic symptoms) secondary to co-trimoxazole.

Final diagnosis: DRESS syndrome.

OUTCOME

The patient developed deranged liver function, with his alanine aminotransferase (ALT) level peaking at 450 IU/L. he was treated with intravenous steroids and his liver function gradually normalised and his rash resolved. The skin biopsy confirmed inflammatory changes consistent with DRESS syndrome. The patient was discharged home on a tapering dose of oral prednisolone. He had one further admission, 4 weeks later, with a rash and fever, but his symptoms were comparatively mild and he did not require intensive care. He was booked in for outpatient allergy testing (to guide future antibiotic treatment plus PCP prophylaxis) and lymphocyte transformation studies. He has remained well since, with no further hospital attendances. He will commence anti-retroviral therapy once his course of prednisolone has been completed.

CASE DISCUSSION

DRESS syndrome is a hypersensitivity reaction that can develop in response to numerous agents, including sulphonamide antimicrobials (present in co-trimoxazole), dapsone, carbamazepine and phenytoin. Patients present with a rash, fever and usually have hepatic involvement, as in this case, although renal and pulmonary complications are also common.

Treatment is usually supportive, with intravenous fluids and topical corticosteroids for the skin lesions. In patients with hepatic involvement, oral corticosteroid therapy may be required. Patients typically develop symptoms of DRESS syndrome several weeks after commencing the causative agent and may have multiple relapses over the subsequent months.

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CASE 80: RENAL FAILURE IN AN INTRAVENOUS DRUG USER

PATIENT HISTORY

A 40-year-old man presented with right leg swelling and a cough on deep inspiration. He was an intravenous drug user who had a long history of injecting into his lower limb veins but more frequently performed 'skin-popping' over recent months due to difficulties with venous access. He felt that over the past few days, his right leg had been increasing in size and was painful to touch. He was now unable to weight-bear on the right leg. He denied any fevers, sweats or weight loss. His past history was significant for chronic left leg venous ulceration and hepatitis C. He drank 50 units of alcohol per week, smoked 30 cigarettes daily and used heroin and crack cocaine several times per week.

EXAMINATION

Initial observations: T 35.9°C, HR 72, BP 92/58 mm Hg, RR 14, SpO₂ 94% on room air.

The patient's chest was clear with no added sounds. Heart sounds were normal and there were no signs of fluid overload. His abdomen was firm but non-tender on palpation. His right leg was swollen, red, warm and tender to touch posteriorly. His left calf had a circumferential ulcer, which had an area of cellulitis with an offensive odour.

INITIAL RESULTS

Bloods: WCC 19, N^o 15.4, Hb 143, Plt 401, Na 130, K haemolysed, creatinine 178, CRP 119.

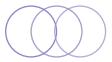
Urine dip: 3+ of protein.

DIFFERENTIAL DIAGNOSIS

A right lower limb deep vein thrombosis is the most probable diagnosis. The patient self-injects into his leg veins and thus is at high risk of thrombus formation. He may well also have a pulmonary embolus given his low oxygen saturations and symptoms of a cough on deep inspiration. An arterial thrombus is another possibility. If thrombus matter is present, this is at risk of becoming infected.

The patient could also have a cutaneous infection, such as cellulitis or an abscess, related to transfer of bacterial pathogens during injection and due to the fact that intravenous drug users often have a degree of immunosuppression. Injection sites around the area should be closely inspected for early signs of necrotising fasciitis.

The patient has an elevated creatinine level – this could represent an acute kidney injury or chronic kidney disease. Tuberculosis with renal involvement or HIV-associated nephropathy both cause chronic renal impairment and the patient is likely to be at risk of acquiring both of these infections.



HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

Intravenous access should be established, although it can be challenging to do so in patients who have undergone excessive venous punctures. Fluid resuscitation should initially be commenced with 0.9% sodium chloride until a serum potassium level is back, at which point compound sodium lactate (Hartmann's solution) can be used if the patient is not hyperkalaemic – this solution contains fewer chloride ions than 0.9% sodium chloride and is therefore less likely to contribute to a hyperchloraemic metabolic acidosis. A septic screen should be carried out, as well as a protein:creatinine ratio to assess the degree of proteinuria.

Either subcutaneous low molecular weight heparin or a novel oral anti-coagulant (NOAC), depending on local guidelines, should be given if deep vein thrombosis is thought to be likely. A Doppler ultrasound of the leg veins should be performed when possible.

You need to consider why the patient may be hyponatraemic – is he intravascularly deplete or could this be pseudohyponatraemia in the presence of hyperlipidaemia. The most probable cause is that the patient is volume depleted (hence his low blood pressure) and the baroreceptor response to this was to increase anti-diuretic hormone release leading to greater water reabsorption from the nephron. A urinary sodium level and paired serum and urinary osmolalities should be tested.

CASE PROGRESSION

The patient was given subcutaneous enoxaparin (dosed at 1.5 mg/kg). A Doppler ultrasound scan of his right leg veins confirmed an extensive deep vein thrombosis (see [Figure 80.1](#)). The team was unable to establish intravenous access and the patient therefore was taken to theatre where an anaesthetist sited a central venous catheter.

Despite intravenous fluids, the patient's renal function deteriorated over the subsequent days, with his creatinine peaking at 450 $\mu\text{mol/L}$ and a refractory hyperkalaemia of 6.9 mmol/L. The patient was transferred to a renal unit for haemodialysis sessions.

An HIV test was negative. Hepatitis C virus antibodies were detected but hepatitis C RNA was not, indicating that the patient had cleared the virus. An autoimmune/vasculitis screen was performed. This identified a hypergammaglobulinaemia.

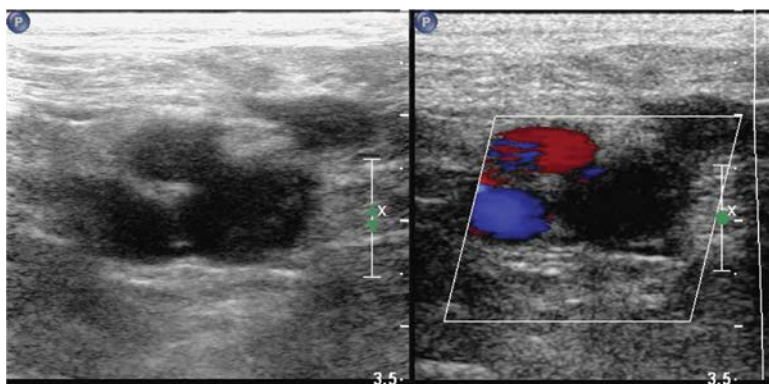


Figure 80.1 Doppler ultrasound scan showing a deep vein thrombosis.



The patient developed signs of cardiac failure and was transferred to the critical care unit for inotropic support. A renal biopsy identified AA amyloidosis.

Final diagnosis: Amyloidosis secondary to intravenous drug use with subsequent renal infiltration.

OUTCOME

The patient remained dialysis-dependent over the subsequent weeks. The plan was to commence immunosuppressive therapy, but the patient developed a hospital-acquired pneumonia and deteriorated further. End-of-life care was commenced and he died 1 week later.

CASE DISCUSSION

Secondary AA amyloidosis is associated with chronic inflammatory conditions, such as rheumatoid arthritis or systemic lupus erythematosus, but is becoming more frequently identified in the intravenous drug using population who often experience recurrent viral and bacterial infections. People who 'skin-pop' in particular are at risk of chronic cutaneous infections. Serum amyloid A protein is an acute phase protein and thus levels rise in the presence of inflammation. Deposition of amyloid A fibrils within the kidneys can lead to renal amyloidosis, presenting with proteinuria and progressing to renal failure.

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CASE 81: DELIRIUM AND TACHYPNOEA

PATIENT HISTORY

An 82-year-old man presented to the emergency department complaining of shortness of breath on exertion, orthopnoea and wheeze. He was a vague historian and was clearly very confused. He did tell the team that he was an ex-smoker, had previously consumed alcohol to excess, and thought that his general practitioner (GP) had stopped a 'water tablet' over the preceding month. Documents on the trust electronic patient record system showed that he had a past history of atrial fibrillation, hypertension, angina and vascular dementia, but no further medical records were available. There were no details for a next-of-kin from whom to take a more complete history. It was a Friday evening and the emergency department team was therefore unable to contact the patient's GP.

EXAMINATION

Initial observations: T 37°C, HR 88 bpm, BP 150/100 mm Hg, RR 28, SpO₂ 95% on room air.

The patient appeared tachypnoeic and agitated. At the time of examination, he was alert and orientated to place and person, but not time, with an Abbreviated Mental Test score (AMTS) of 7/10 (points lost for concentration, recall, and naming the year). Respiratory examination identified reduced air entry bilaterally and widespread wheeze. He had an irregular heartbeat and pitting oedema to the ankles, but his jugular venous pressure (JVP) was not elevated. Abdominal examination was unremarkable. No focal neurological abnormalities were identified.

INITIAL RESULTS

Routine blood tests: WCC 7.6, Hb 138, Plt 161, Na 140, K 4.0, Urea 5.6, Creat 83, CRP 4.

Liver function tests were normal.

Electrocardiogram (ECG): atrial fibrillation, rate 80–110 bpm.

DIFFERENTIAL DIAGNOSES

Although he has known vascular dementia, the patient's confusion appears to have improved somewhat during the examination, as he was noted to be very confused on admission but achieved 7/10 marks on the AMTS. Fluctuating confusion is typical for delirium. He may have an underlying infection that has precipitated the onset of delirium. Based on his smoking history, shortness of breath, tachypnoea and wheeze, an infective exacerbation of chronic obstructive pulmonary disease (COPD) seems likely, although other infections should be considered.

If his GP has recently stopped a diuretic, it may be that the patient has experienced worsening of his heart failure symptoms, with pulmonary oedema developing. If the patient has developed new-onset atrial fibrillation, this may also lead to worsening heart failure.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

A chest x-ray should be performed to look for potential causes of the patient's respiratory symptoms, such as consolidation or pulmonary oedema. Depending on the findings, antibiotics or diuretics may be considered.

An arterial blood gas will allow you to assess his acid-base status, potentially identifying a longstanding respiratory acidosis with metabolic compensation (indicative of chronic lung disease) or an acute respiratory or metabolic acidosis.

A collateral history is essential to establish whether this is the patient's baseline cognitive function or whether he has deteriorated acutely. Further information on his social situation is also required. Often, calling the medical or emergency department teams at other local hospitals may allow you to obtain more information, particularly if electronic letters or discharge summaries are available.

CASE PROGRESSION

Shortly after the initial examination, the patient became tachycardic with a heart rate of 110–120 bpm. The chest x-ray showed cardiomegaly and interstitial oedema and the patient was subsequently diagnosed with worsening congestive cardiac failure secondary to atrial fibrillation with intermittent rapid ventricular rate and cessation of oral diuretic therapy.

Twelve hours later, the patient was re-examined and was found to have sacral oedema present. Oral furosemide and digoxin were commenced. His listed GP was available on Saturday morning, but he explained that the patient had not attended the surgery for more than 10 years and had moved to another (unknown) practice. No next-of-kin details were available.

On day 2 of his admission, the patient had a small (<10 mL) rectal bleed. Digital rectal examination found haemorrhoids and soft brown stool in the rectum. The patient was wandering around the ward in a confused state. His mini-mental state examination (MMSE) score was 18/30. His white cell count had risen to $20.9 \times 10^9/\text{L}$. Later that evening, a nursing assistant documented that the patient had an episode of diarrhoea and the ward nurses stated that the patient had begun smearing faeces around the ward.

On day 4, the patient's white cell count had risen to $23 \times 10^9/\text{L}$ and his C-reactive protein (CRP) was now 314 mg/L. A full confusion screen, including a computed tomography (CT) head scan, did not identify an acute precipitant for the patient's deterioration. No source of infection was identified on examination so antibiotics were held off. The septic screen was repeated and an echocardiogram was requested to assess his cardiac function.

On day 5, the patient became agitated and dyspnoeic overnight. An abdominal x-ray showed dilated loops of small bowel and a prominent large bowel (see [Figure 81.1](#)). Digital rectal examination found liquid stool. An arterial blood gas showed a metabolic acidosis with a lactate level of 7.4 mmol/L (reference range 0.5–2.2 mmol/L). The surgical team reviewed the patient and noted abdominal guarding. They thought the likely diagnosis was infective diarrhoea (possibly due to *Clostridium difficile* infection).

Several hours later, he developed a distended abdomen and cold peripherae. He passed liquid faeces twice. The critical care team reviewed and commenced co-amoxiclav and metronidazole. Later that night, the patient had an episode of profound hypotension, vomited and compromised

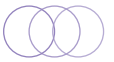


Figure 81.1 An abdominal x-ray showing dilated loops of small bowel and a prominent large bowel.

his airway. He was ventilated on the intensive treatment unit, where a diagnosis of ischaemic colitis was made. The patient continued to deteriorate over the next 48 hours and died.

Final diagnosis: Ischaemic colitis.

OUTCOME

Following a post-mortem examination, the coroner reported that the cause of death was ischaemic colitis and sepsis, presumably secondary to atrial fibrillation-related thromboemboli.

CASE DISCUSSION

Ischaemic colitis is caused by a reduction in intestinal blood flow, usually due to occlusion or vasospasm. Patients develop bowel infarction, leading to profound sepsis and subsequent circulatory collapse.

This case highlights the importance of obtaining a collateral history when a patient presents in a confused state, particularly where a diagnosis of dementia exists. It is difficult to make assessments regarding escalation of care, or simply to know what a patient's baseline function is and whether they are delirious without discussion with family, carers and healthcare workers. This patient was unlikely to be a suitable candidate for surgery, even at the time of admission, due to his poor baseline function.

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CASE 82: POST-PARTUM AUDITORY HALLUCINATIONS

PATIENT HISTORY

A 24-year-old South-Asian woman was brought to hospital by her husband who was concerned that for the preceding 48 hours she had developed auditory hallucinations and religious preoccupations. She was 6 weeks post-partum, having delivered a healthy baby that she was currently breastfeeding. She had no past medical history. She lived with her family and did not smoke or drink alcohol.

EXAMINATION

Initial observations: T 37.1°C, HR 110, BP 118/80, RR 16, SpO₂ 100% on room air.

Systems examination was unremarkable.

INITIAL RESULTS

Routine blood tests: WCC 8.1, Hb 107, PLT 249, Na 139, K 3.9, Creat 65 and CRP 81.

DIFFERENTIAL DIAGNOSES

The patient appears to be experiencing post-partum psychosis, which is a severe episode of depression or mania, often with confusion, hallucinations, paranoia or delusions. The condition begins in the first few weeks post-partum.

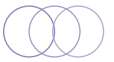
The patient may have developed delirium secondary to an infection, such as mastitis or a urinary tract infection. The history does not state whether she had a vaginal delivery or a Caesarean section, which may provide useful information when investigating for potential sources of infection.

Post-partum thyroiditis is an autoimmune condition that presents within the first six months post-childbirth, classically with thyrotoxicosis initially, followed by a period of hypothyroidism, with most women becoming euthyroid within 12–18 months of onset of symptoms.

Lastly, as with all patients presenting with altered mental state, encephalitis should be considered, with viral and bacterial causes being most likely.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

An urgent computed tomography (CT) scan of the brain should be performed to look for intracranial pathology. Antibiotic and anti-viral cover should be given for possible encephalitis and a lumbar puncture should be performed as soon as possible.



A septic screen should take place, and blood tests will need to be sent for corrected calcium and thyrotropin (TSH) levels, both of which may cause confusion when deranged. An autoimmune screen should also be sent, as cerebral vasculitis is a possible diagnosis.

The psychiatry liaison doctors and nurses, ideally from a specialist peri-partum team, should be contacted to provide support with the management of this patient.

CASE PROGRESSION

The patient remained agitated and became distressed when she was prevented from trying to communicate her religious beliefs to other patients. A CT head scan showed an enlarged pituitary gland, in keeping with her recent pregnancy. A lumbar puncture was performed and cerebrospinal fluid (CSF) values were all unremarkable. No infection or electrolyte abnormalities were detected. The patient was referred to the psychiatry team who commenced regular haloperidol for probable post-partum psychosis.

Blood tests showed hyperthyroidism: TSH 0.03 (ref. range 0.27–4.2 mIU/L), free T4 33.6 (reference range 12.0–22.0 pmol/L) and free T3 8.4 (ref. range 3.1–6.8 pmol/L). Anti-thyroid peroxidase (anti-TPO) antibodies were strongly positive at 659 (ref. range 0–150 U/mL), as were her anti-thyroglobulin antibodies at 1092 (reference range 0–150 U/mL). The endocrinology team reviewed the patient and diagnosed thyroiditis. Propranolol was commenced to control her tachycardia.

A magnetic resonance imaging (MRI) brain scan was subsequently performed, showing pituitary hyperplasia. A pituitary hormone screen was carried out, which was significant for a low IGF-1 level of 3.5 (ref. range 13–50 nmol/L) and an adrenocorticotrophic hormone (ACTH) level of <5 (ref. range <46 ng/L) with a 9 AM cortisol of <5 (reference range 171–536 nmol/L). On direct questioning, the patient's husband disclosed that patient used skin lightening creams daily. He brought in the jar of cream and it was found to contain corticosteroids. This was felt to have partly contributed to her adrenal suppression. Oral hydrocortisone therapy was commenced.

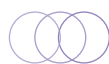
Final diagnosis: Multiple post-partum endocrinopathies: thyroiditis, hypophysitis and probable corticosteroid-induced adrenal suppression.

OUTCOME

Following hydrocortisone therapy and initiation of beta blockade, the patient improved symptomatically and her hallucinations and elusions resolved. She was followed up as an outpatient in the endocrine clinic and was subsequently found to have developed primary hypothyroidism. She is currently taking thyroxine and is being reviewed regularly as an outpatient.

CASE DISCUSSION

Both hypophysitis and thyroiditis presenting as overt disease in the post-partum phase are well recognised. It has been previously reported that patients with autoimmune thyroiditis



may also have anterior pituitary antibodies without clinical signs or symptoms, and vice versa. To develop both autoimmune endocrinopathies simultaneously, however, is highly unusual, and may suggest an associated underlying immune process. This interesting case of a woman presenting with features of both post-partum thyroiditis and hypophysitis highlights the importance of considering multiple endocrine pathologies during this period, particularly in the context of autoimmunity. It also demonstrates the complexities and challenges of investigating and managing such cases well.

With thanks to Drs Tómas Agustsson, Danielle Lewis, Dulmini Karyiawasam and Stephen Thomas.

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CASE 83: SHIVERING AT THE STATION

PATIENT HISTORY

A 19-year-old woman was brought to the emergency department in early February. She had been found shivering in the bathroom at London Bridge station at 5 AM by a station attendant. She explained on the preceding day she had travelled from Edinburgh to London by coach and was planning to travel on to Paris, but had missed her connection and therefore opted to spend the night at the station. Her main complaint was of bilateral calf tenderness (left more than right). She had no past medical history and took no regular medications. She was a university student and lived in halls of residence. She smoked five cigarettes daily and drank around 15 units of alcohol per week.

EXAMINATION

Initial observations: T 31.4°C, HR 114 bpm, BP 150/90 mm Hg, RR 20, SpO₂ 97% on room air. The patient was noted to be of slim build and felt cold to touch. She had a capillary refill time (CRT) of 6 seconds and swollen, tender calves bilaterally (left more than right).

INITIAL RESULTS

Routine blood tests: WCC 31.4, N^o 27.6, Hb 137, PLT 480, Na 133, K 6.4, Creat 37, CRP 5, CK 660, D-dimer 0.4 and INR 1.2.

Urine dip: 2+ blood, 2+ protein.

Venous blood gas: pH 6.89, pCO₂ 3.5, HCO₃ 4.9, BE -27, lactate 17 and anion gap 27.

DIFFERENTIAL DIAGNOSES

The patient has a profound metabolic acidosis with a high anion gap (>11 mEq/L). Possible causes for this include methanol and ethylene glycol toxicity and salicylate overdose. The most probable cause in this case is the patient's severe hyperlactataemia. Diabetic ketoacidosis is another potential cause of metabolic acidosis with a high anion gap, although you would expect to see ketones in the patient's urine dip. Nevertheless, a blood ketone and plasma glucose level should be sent to exclude this important diagnosis.

The patient may have severe sepsis, presenting with hypothermia, metabolic acidosis and a neutrophilia. A full septic screen will be required to identify potential foci of infection.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient will need to be examined thoroughly looking for potential foci of infection and a full septic screen should be carried out. Blood tests should be sent to check the levels of

salicylates, ethanol, cortisol and thyrotropin (TSH). A blood film should also be performed to exclude an acute leukaemia, in view of the elevated white cell count.

The patient will need to be warmed slowly at 0.5°C–1°C per hour, using multiple blankets, warm drinks and a warming blanket (e.g. Bair hugger). She should be kept on a cardiac monitor, as hypothermia can precipitate cardiac arrhythmias.

She should be given intravenous sodium bicarbonate initially, followed by warmed saline. Her acid–base status and electrolytes will need to be closely monitored and she should be managed in a high dependency unit setting.

CASE PROGRESSION

The patient was warmed to 34°C using a Bair hugger. Intravenous sodium bicarbonate was given until the base excess reached –3. Insulin and dextrose treatment helped to correct the hyperkalaemia. Intravenous co-amoxiclav was commenced for possible sepsis of unknown source. Intravenous pabrinex was started for possible alcohol misuse. She was admitted directly to the high dependency unit.

Central and arterial lines were inserted. She was slowly warmed and rehydrated. Her lactic acidosis resolved over 24 hours. A computed tomography (CT) scan of the pulmonary arteries showed no evidence of pulmonary embolism (suspected because of the profound acidosis, tachycardia and calf-swelling that could represent deep vein thrombosis).

Her care was transferred to the medical ward. A Doppler ultrasound scan of her calves showed no deep vein thromboses. She continued to complain of calf pain. A magnetic resonance imaging (MRI) scan of her legs was arranged, which showed bilateral oedema, predominantly in the left calf, likely to represent myositis/cold necrosis (see [Figures 83.1](#) and

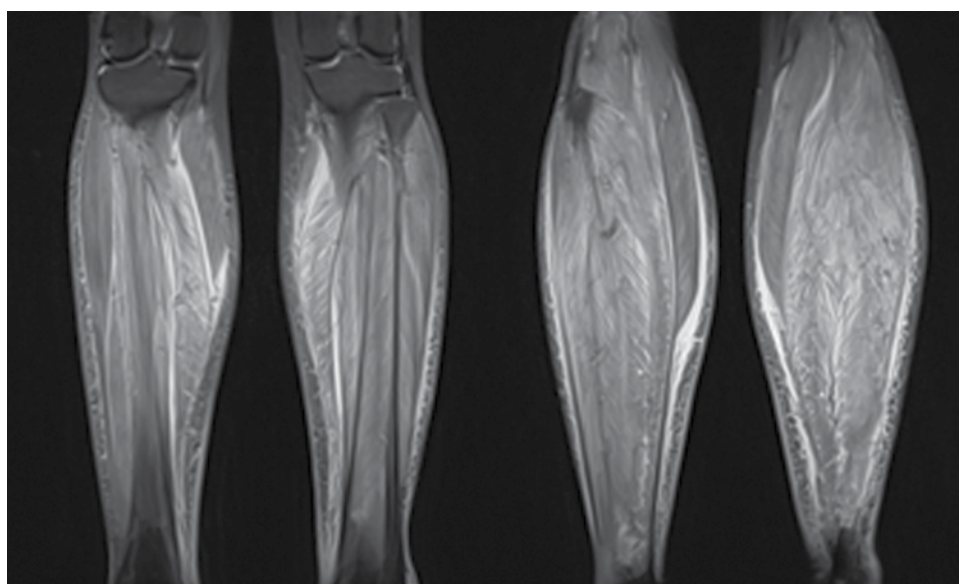


Figure 83.1 MRI scan showing oedema of the calf muscles.

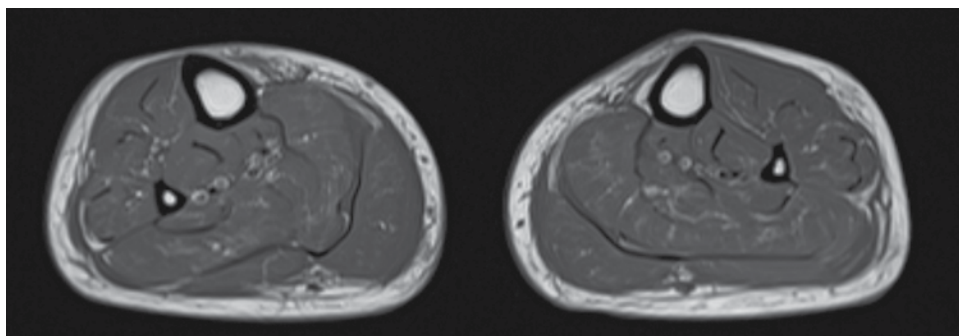
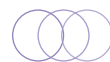


Figure 83.2 MRI scan showing oedema of the calf muscles.

83.2). The plastic surgery team reviewed and recommended conservative management. Her creatine kinase (CK) peaked at 4345 and then settled over the following days.

Final diagnosis: Hypothermia-induced myopathy.

OUTCOME

The patient required intensive physiotherapy for several days before she was fit to travel back to Edinburgh.

CASE DISCUSSION

The patient was profoundly hypothermic and had spent hours shivering in the station bathroom. The elevated CK level and the urine dip showing 2+ blood are features of rhabdomyolysis, which likely developed following prolonged shivering.

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CASE 84: NOCTURNAL ENURESIS AND BACK PAIN

PATIENT HISTORY

A 34-year-old woman walked into emergency department at 8 PM complaining of severe back pain. She had experienced progressive lower back pain over the preceding 3 months, which she felt was associated with her increased exercise schedule, as she was currently training to run a marathon. On direct questioning, she described urinary frequency and nocturnal urinary incontinence and also mentioned that she had intermittent 'pins and needles' sensations in her right foot. She had been seen several times in the urinary incontinence clinic where investigations had not identified a cause for her symptoms and the impression was that the patient may have psychogenic polydipsia. Her past history included recurrent urinary tract infections, including an episode of pyelonephritis 2 years earlier, which had presented with back pain. She took no regular medications, did not drink alcohol or smoke, and was in a long-term monogamous relationship with a male partner. She worked as an apprentice at an investment banking company and had only travelled to New York and Hawaii in the preceding year.

EXAMINATION

Initial observations: T 36.8°C, HR 76 bpm, BP 110/76 mm Hg, RR 16, SpO₂ 99% on room air.

Systems examination was documented as normal aside from reduced power (3/5) on hip flexion and hip extension in the right lower limb.

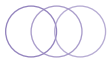
INITIAL RESULTS

Routine blood tests: WCC 11.1, Hb 142, Plt 407, Na 141, K 3.6, Creat 46, Bili 35, ALT 21, ALP 40, CRP 3, INR 0.9.

Urine dip: 3+ leucocytes; nitrite +ve, βHCG –ve.

DIFFERENTIAL DIAGNOSES

Spinal cord compression with cauda equina syndrome is the most important diagnosis to exclude. Patients present with back pain, progressive lower limb weakness and retention or incontinence of urine +/- faeces. The examination did not appear to include an assessment for possible altered sensation around the perineum, buttocks and inner thighs (saddle anaesthesia) or for reduced anal tone, both of which would support a diagnosis of cauda equina syndrome. In a young patient who exercises frequently, disc prolapse would be the most probable cause of spinal cord compression. Discitis, from an infection such as *Mycobacterium tuberculosis*, or *Escherichia coli* or *Proteus* species, in view of the patient's history of recurrent urinary tract infections is another possible diagnosis. A primary spinal tumour or metastatic spinal deposits from a primary malignancy such as cervical or breast cancer should also be considered.



The history of intermittent pins and needles sensations in her right foot and urinary incontinence is in keeping with a first presentation of multiple sclerosis.

The patient may have pyelonephritis, causing additional discomfort in addition to her exercise-induced back pain. She has leucocytes and nitrite present in her urine and a mildly elevated white cell count. This diagnosis should be considered, but it is important to exclude the above, potentially more serious, conditions.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient needs an urgent magnetic resonance imaging (MRI) scan of her spine, looking for spinal cord compression and cauda equina syndrome. Further management will be entirely dependent on the results of this investigation.

CASE PROGRESSION

Antibiotics were commenced for a presumed urinary tract infection. A renal ultrasound scan was performed in the emergency department and no abnormalities were seen. A lumbar spine x-ray was unremarkable. A computed tomography (CT) head was also performed with no acute pathology seen. The emergency department team arranged an MRI scan of the whole spine to be performed the following morning and the patient was admitted under the medics for further investigations.

The next morning, when she was reviewed by the medical consultant, further history was elicited. She described progressive weakness of the right leg and episodes of collapse, where her right leg would give way when running. On examination, she had proximal lower limb weakness (right more than left), brisk knee reflexes in the right leg and the right plantar was up-going (left plantar equivocal).

The MRI scan was initially reported as showing a very large, sacculated syrinx which involved almost the entire cord, extending from the C4 level to L1/2, at which point there was particular cord expansion (see [Figure 84.1](#)). The patient was referred to the neurosurgeons, who planned to take over care of the patient later that week. The scan was subsequently reviewed by a specialist neuroradiologist and the impression was that the abnormality actually represented a spinal cord tumour, such as an astrocytoma or ependymoma. She was transferred to the local neurosurgical team for urgent intervention later that day.

Final diagnosis: Spinal cord tumour.

OUTCOME

The patient underwent total resection of the tumour and a laminectomy. A complete curative excision is thought to have been achieved. Her urinary and neurological symptoms have since resolved fully. She will be followed up by the neurosurgical team.



Figure 84.1 MRI spine scan showing the spinal cord tumour.

CASE DISCUSSION

This case demonstrates the importance of a thorough neurological examination to ensure the correct signs are identified. In patients presenting with features of cauda equina, an urgent MRI scan of the spine should be arranged to allow timely surgical intervention.

The patient had a spinal ependymoma, which is a slow-growing intramedullary neoplasm with a good prognosis where complete excision is possible (5-year survival rate 85%).

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CASE 85: FEVER AND COUGH (PART 2)

PATIENT HISTORY

A 56-year-old man was admitted from the HIV outpatient clinic complaining of fever and shortness of breath. He described shortness of breath on exertion and a new cough productive of yellow sputum with streaks of blood. He felt nauseated and generally weak. His past medical history included a hospital admission 6 weeks earlier where he had been diagnosed with pulmonary tuberculosis and tested positive for HIV at that time. His CD4 count at that point had been 9 (reference range 450–1660 cells/mm³). Anti-tuberculosis treatment was commenced at this stage, followed by anti-retroviral therapy, and co-trimoxazole for *Pneumocystis jirovecii* pneumonia (PCP) prophylaxis 2 weeks later. He took no other medications. He did not drink alcohol and had never smoked. He worked as a bus driver and lived with his son. He was originally from Nigeria and had lived in the United Kingdom for the past 3 years with annual holidays to Nigeria.

EXAMINATION

Initial observations: T 37.7°C, HR 92 bpm, BP 120/78 mm Hg, RR 20 and SpO₂ 97% on room air.

The patient appeared dyspnoeic on minimal exertion. He was warm and well perfused. His chest had crackles at the right mid zone. His abdomen was soft and non-tender. There was cervical and inguinal lymphadenopathy with soft, mobile nodes of <10 mm diameter.

INITIAL RESULTS

Routine blood tests: WCC 14.7, N^o 12.0, L^o 2.3, Hb 137, Plt 400, Na 138, K 43, Creat 210 (baseline 170), CRP 82.

DIFFERENTIAL DIAGNOSES

The patient has presented with fever, cough and shortness of breath on a background of recently being diagnosed as positive for HIV with pulmonary tuberculosis 5 weeks earlier. He could have community-acquired pneumonia (either viral or bacterial) or may have developed an opportunistic infection related to his history of immunosuppression, such as PCP.

The patient's pulmonary tuberculosis may not have responded to treatment with quadruple therapy (isoniazid, rifampicin, pyrazinamide and ethambutol) if the patient has not adhered to the therapy, or if he has contracted either a resistant form of *Mycobacterium tuberculosis*, or an atypical tuberculosis infection, such as *Mycobacterium avium-intracellulare*.

Alternatively, he may be experiencing an immune reconstitution inflammatory syndrome (IRIS), whereby a severe inflammatory reaction against a previously acquired pathogen occurs following an improvement in immune function. This can develop after initiation of anti-retroviral therapy or commencing a different anti-retroviral regime.



HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

A full septic screen should be carried out, including blood and sputum cultures and a chest x-ray. Sputum should additionally be sent for PCP analysis and acid-fast bacilli. As the patient is already on quadruple therapy, the case should be discussed with the on-call infectious diseases team to decide whether further antimicrobial therapy is needed, and if so, which agent would be most appropriate to commence. Ideally, a specialist HIV team will provide further advice on the management of this patient.

CASE PROGRESSION

The patient was reviewed by the HIV and infectious diseases teams. Further blood tests identified that the patient also had an acute hepatitis. It was initially unclear whether this was the result of drug-induced hepatotoxicity (secondary to his recently commenced medications) or tuberculosis-IRIS. He complained of blurred vision and fundoscopy was consistent with cytomegalovirus (CMV) retinitis.

The patient was diagnosed with IRIS (leading to both IRIS-tuberculosis and reactivation of CMV) and subsequently commenced prednisolone and montelukast to suppress the severe inflammatory response.

Final diagnosis: IRIS.

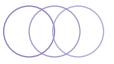
OUTCOME

The patient had widespread lymphadenopathy on a computed tomography (CT) scan of his chest, which regressed following initiation of immunosuppressive therapy. Both his anti-tuberculosis and anti-retroviral medication regimes were continued throughout. Over the next 3 weeks, he made a gradual recovery and was discharged home. He has since remained well and has completed his course of anti-tuberculosis treatment.

CASE DISCUSSION

IRIS occurs following an improvement in immune function in patients with previous long-standing immunosuppression. Undiagnosed opportunistic infections may become apparent as an inflammatory response to the pathogen is generated or there may be a clinical deterioration in a partially treated infection, such as in this case.

Patients with IRIS are usually managed by specialist HIV or infectious diseases physicians. In severe cases, corticosteroid treatment may be considered, although this will increase the risk of developing further infections. Anti-retroviral therapy is usually continued during IRIS, although in certain cases, particularly in patients with cryptococcal meningitis, this may be adjusted or even stopped.



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CASE 86: UNCONSCIOUS OUTSIDE A CLUB

PATIENT HISTORY

A 24-year-old man was found slumped on the steps outside a club by his friends, who called an ambulance. When the paramedics arrived they found his Glasgow Coma Scale (GCS) to be 3 (E1, V1, M1) and his pupils to be dilated at 6 mm bilaterally and sluggish. He became intermittently apnoeic during the assessment and a laryngeal mask airway was sited. He was brought to the emergency department where he was intubated. The friend accompanying him stated that the patient had consumed several alcoholic drinks that night and regularly used the psychoactive drug, γ -hydroxybutyric acid (GHB).

EXAMINATION

Initial observations while intubated and ventilated: T 37.4°C, HR 130 bpm, BP 122/80 mm Hg.

The patient was unresponsive, receiving propofol and fentanyl sedation. His heart sounds were normal and he was warm and well perfused. His chest was clear to auscultation. His abdomen was soft and bowel sounds were quiet. His pupils were now 4 mm and reactive to light bilaterally.

INITIAL RESULTS

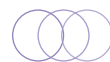
Routine blood tests: WCC 15.8, N^o 12.1, Hb 130, Plt 210, Na 135, K 2.9, Creat 119, CRP <1, capillary glucose 3.0, ethanol <100 mg/L.

Arterial blood gas (intubated and ventilated): pH 6.5, pO₂ 17.2, pCO₂ 4.0, BE -36. HCO₃ 4, lactate 1.4.

Calculated anion gap: 46 (normal anion gap: 3–11 mEq/L).

DIFFERENTIAL DIAGNOSES

The patient has a history of using recreational drugs and was drinking alcohol prior to his presentation. The most striking result is the blood gas, which shows a profound metabolic acidosis and a raised anion gap. Potential causes of this include alcoholic ketoacidosis, ingestion of toxins (including toxic alcohols, such as ethylene glycol or methanol) or an overdose of aspirin (acetylsalicylic acid). There is no evidence that the patient has a lactic acidosis or diabetic ketoacidosis. The patient may be experiencing the sedative effects of GHB in addition to excess alcohol, possibly with other recreational drugs. He also has an apparent acute kidney injury, possibly due to rhabdomyolysis or induced by recreational drugs/other toxins.



HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient will require care on an intensive treatment unit. Depending on whether his metabolic acidosis is resolving, and if so how rapidly, he may require renal replacement therapy (RRT). Organ support will be given to maintain his respiratory and cardiovascular function.

CASE PROGRESSION

The patient had already received 3000 mL compound sodium lactate plus 500 mL 1.26% sodium bicarbonate in the emergency department and was passing large volumes of urine. He was transferred to the intensive treatment unit where a dialysis-type central venous catheter (vascath) was sited and RRT was commenced. He was given a further 100 mL of 8.4% sodium bicarbonate followed by fluid challenges with Plasma-lyte (crystalloid solution) and replacement of electrolytes. A noradrenaline infusion was titrated to keep his mean arterial pressure at 65–70 mm Hg. Over the next 12 hours, the patient's creatinine level rose to 180 $\mu\text{mol/L}$ and the metabolic acidosis improved slightly (pH 7.0, HCO_3^- 15). He was noted to have moderate erythema and oedema of the lips and tongue, possibly due to irritant effects of a substance consumed before admission or an angioedema reaction.

A specialist toxicology team reviewed the patient. They noted that sedation was likely due to GHB and alcohol intake and that the patient may be experiencing toxicity from additional recreational drugs. The profound metabolic acidosis with a large anion gap had persisted and the toxicology team recommended that a fomepizole infusion be commenced as an antidote for presumed toxic alcohol ingestion and that blood samples be sent for toxicological analysis.

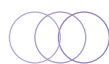
Thirty-six hours later, the toxicology laboratory found that levels of methanol and ethylene glycol measured in the blood samples were undetectable and the fomepizole infusion was therefore stopped. There was no obvious cause for the raised anion gap metabolic acidosis, which was gradually resolving on RRT. The doses of sedative agents were weaned and the patient became more alert, although he was unable to be extubated due to concerns regarding his oral/airway oedema making re-intubation challenging, should this be required, or progressing to cause airway obstruction.

Methanol is metabolised to formaldehyde then formic acid. The toxicology team postulated that when the blood samples were taken, the patient may have already metabolised the methanol. They tested the sample for formic acid and it came back strongly positive, indicating that the patient's profound metabolic acidosis and impaired consciousness level were due to methanol toxicity.

Final diagnosis: Methanol toxicity.

OUTCOME

The patient was extubated after spending 4 days in the intensive treatment unit. He denied deliberately ingesting methanol and stated that the only recreational drugs that he had used recently were cocaine and GHB, although he had purchased some cheap alcohol from an



acquaintance that he consumed in the hours prior to his collapse (isolated cases of methanol being substituted for ethanol in home-brew drinks have been reported).

CASE DISCUSSION

Methanol is found in antifreeze and windscreen wiper solutions, paint remover and photocopy machine diluents. Methanol toxicity typically presents with nausea and vomiting, followed by a reduced consciousness level. A profound metabolic acidosis with a raised anion gap can develop, as occurred in this case. Sodium bicarbonate is given to correct the acidosis, but RRT is required in severe cases.

Fomepizole is a competitive inhibitor of alcohol dehydrogenase and its administration will slow the metabolism of methanol and thus the rate of formaldehyde/formic acid production. Intravenous folinic acid may be given to enhance formic acid degradation. Care is otherwise supportive. Patients may develop permanent visual damage following methanol-induced retinal/optic nerve oedema and subsequent optic nerve demyelination, as well as damage to the basal ganglia.

With thanks to Dr Takahiro Yamamoto for his assistance with this case.

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CASE 87: FEVERS, NIGHT SWEATS AND LYMPHADENOPATHY

PATIENT HISTORY

A 21-year-old woman presented to the emergency department complaining of a 6-week history of painful lumps in her neck. She had noticed two large lymph nodes in the right anterior cervical triangle, which were tender to touch and were increasing in size. For the preceding fortnight, she had experienced fevers and drenching night sweats. She felt fatigued and thought that she may have lost weight unintentionally. She denied any symptoms of cough or joint pain. She had no significant past medical history and took no regular medications. She was born in Sri Lanka and had lived there until she was 11 years of age; she continued to visit her grandparents there every year. She worked as a delivery driver and did not smoke, drink alcohol or use recreational drugs. She had no recent sexual partners.

EXAMINATION

Initial observations: T 39.9°C, HR 90 bpm, BP 108/76 mm Hg, RR 18, SpO₂ 100% on room air.

The patient appeared clinically well at rest. Her chest was clear and her heart sounds were normal. Her abdomen was soft, with palpable hepatomegaly of 1 cm below the costal margin. There was cervical lymphadenopathy present, with a 2.5 cm right-sided submandibular node and a 1 cm submental node present. An erythematous rash was present over her cheeks. No axillary or inguinal nodes were palpated. There were no rashes and there was no oral candidiasis.

INITIAL RESULTS

Routine blood tests: WCC 3.4, N° 2.0, L° 0.4, Hb 108, MCV 80, Plt 255, Na 138, K 4.2, Creat 88, CRP 80.

DIFFERENTIAL DIAGNOSES

The patient has developed fevers, cervical lymphadenopathy, night sweats and weight loss.

Hodgkin's lymphoma should be considered as one of the primary differential diagnoses and typically presents either in early adulthood or in adults over the age of 60 years. Non-Hodgkin's lymphoma can develop in younger adults but is uncommon.

Tuberculosis is the other major differential diagnosis in this patient who regularly spends time in South Asia. All of her symptoms are consistent with a *Mycobacterium tuberculosis* infection. The history does not mention whether she has any unwell contacts. She may also have infection with non-tuberculous *Mycobacterium*, such as *M. bovis* from consuming milk in Sri Lanka.

Infectious mononucleosis (due to Epstein–Barr virus [EBV], cytomegalovirus [CMV], toxoplasmosis or HIV seroconversion) could present in this manner and these infectious agents



should be included in the differential. Although no obvious risk factors for acquiring HIV infection have been identified, she should certainly be tested for this and syphilis. If she had established HIV infection then Castleman's disease or Kaposi's sarcoma could also present in this manner.

A history of travel to the United States should be taken in case of possibility of ulceroglandular tularaemia.

Solid malignancies, such as head and neck, or oral cancer, should be considered. The patient does not have symptoms of dysphagia, odynophagia, dyspnoea or ear pain, but some cases of head and neck cancer may simply present with painless cervical lymphadenopathy.

Throat examination is important as tonsillitis may be associated with all the features described, though the duration of illness makes this less likely.

Other rare diagnoses include sinus histiocytosis with massive lymphadenopathy (SHML), Kimura disease, Kikuchi's disease and IgG4 disease. These would all be possible diagnoses to be established on histology of the lymph node. The patient is 21 and of Asian origin so Kimura and Kikuchi's would be possible diagnoses as both are more common in such a population.

Sarcoidosis is possible and a chest x-ray would be required to determine if hilar lymphadenopathy is also present.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

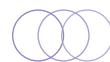
The patient will need a chest x-ray to look for signs of infection (particularly pulmonary tuberculosis), hilar lymphadenopathy or pulmonary metastases. Blood cultures should be taken, as well as respiratory viral swabs. She is currently haemodynamically stable, well hydrated and tolerating oral intake so intravenous fluids are not required.

Where possible, an urgent excision biopsy of lymph node tissue should be performed to allow histopathological analysis. Alternatively, if this is not possible, then an interim fine-needle aspiration (FNA) could be performed, though biopsy may still be later required if this fails to clearly demonstrate an alternative diagnosis. Depending on how quickly a biopsy can be performed and when results are likely to be available, a computed tomography (CT) scan of the patient's neck, chest, abdomen and pelvis may also be considered to identify potential malignancy (and enable staging of this).

Broad-spectrum antibiotics can be withheld at present (unless tonsillitis is seen on examination), as lymphoma and tuberculosis are the two primary differential diagnoses, and it is imperative to obtain a tissue sample for culture prior to commencing anti-tuberculosis antibiotics in case of antibiotic resistance. It is, however, safe to give beta-lactams or macrolides if concern is present of tonsillar infection. The case should be referred to the local respiratory and infectious diseases teams.

CASE PROGRESSION

The patient was admitted under the medical team for further investigations. She was reviewed by the haematology team who felt that lymphoma was the most probable diagnosis. They arranged for an urgent cervical lymph node biopsy to be performed the next day. The



respiratory team also saw the patient and considered tuberculosis to be more likely; they were aiming to commence anti-tuberculosis therapy once the biopsy tissue had been sent for culture of acid-fast bacilli.

A CT scan of the patient's neck, chest, abdomen and pelvis showed widespread lymphadenopathy, with cervical, hilar, axillary and inguinal lymphadenopathy present, consistent with lymphoma. Allopurinol was commenced at this point, as prophylactic treatment of possible tumour lysis syndrome (which may develop once chemotherapy is commenced).

Surprisingly, the histology report was consistent with neither lymphoma nor tuberculosis. There were no Reed–Sternberg cells present (indicative of lymphoma). Histological analysis showed extensive necrosis with large numbers of T lymphocytes and reactive histiocytes. The findings were consistent with Kikuchi disease. Acid-fast bacilli (AFB) culture was completed at 8 weeks and did not reveal any mycobacteria supporting this diagnosis.

Final diagnosis: Kikuchi disease.

OUTCOME

The patient was treated with a course of oral prednisolone and her symptoms were managed with simple analgesia. She was discharged home 2 days later and made a steady recovery over the subsequent fortnight. She remains well without symptoms.

CASE DISCUSSION

Kikuchi disease, otherwise known as histiocytic necrotising lymphadenitis, is a condition that primarily affects young adults of Asian ethnicity, particularly Japanese people. Symptoms and signs can be difficult to distinguish from lymphoma or tuberculosis, or systemic lupus erythematosus in some cases, with the diagnosis often only being established once histopathology results are available. Treatment is typically supportive, although corticosteroids may be warranted in patients with moderate symptoms. Immunosuppressant agents may be required in severe cases.

The underlying aetiology of the condition is unclear, with no specific infections or genetic variations being identified as a potential cause. Some specialists suggest that Kikuchi disease is a hyperimmune response to a variety of stimuli in genetically predisposed individuals.

With thanks to Dr Mukunthan Srikantharajah for his assistance with this case.

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CASE 88: HEADACHE AND JAW PAIN

PATIENT HISTORY

A 68-year-old man presented to the emergency department complaining of a 2-day history of gradual-onset generalised headache, which he had never had before. It was described as a 'strong pressure' over the entire head and he said it felt 'as though my head will explode'. The pain initially developed following a long spell outdoors in the cold weather. There were no exacerbating or relieving features. The headache was associated with left-sided facial numbness and tingling around the mandible. He complained that the left side of the face felt 'congested' and was tender to touch. He denied scalp tenderness but did have some jaw pain when he chewed food. His past medical history included lung adenocarcinoma, which was diagnosed 6 years ago and treated (with curative intent) with a lobectomy. His history also included rheumatoid arthritis, which was diagnosed 30 years ago and was previously managed with methotrexate. This had been well controlled until recent weeks when he had noted morning stiffness and widespread joint pain. He used a long-acting tiotropium inhaler and took 10 mg lercanidipine once daily. He was a retired welder and lived with his female partner. He stopped smoking 6 years ago and had an 80 pack year history. He drank 8 units of alcohol per week.

EXAMINATION

Initial observations: T 36.8°C, HR 80 bpm, BP 130/88 mm Hg, RR 16, SpO₂ 96% on room air. Systems examination, including a full neurological examination was unremarkable.

INITIAL RESULTS

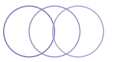
Routine blood tests: WCC 10.8, N° 6.6, Hb 129, Plt 160, Na 137, K 3.7, Creat 70, CRP 10.

DIFFERENTIAL DIAGNOSES

The patient presents with headache, left-sided facial numbness and jaw pain. Giant cell arteritis is the main diagnosis to exclude. This is a vasculitis of the temporal arteries that tends to affect people in their sixth to eighth decades of life. Symptoms include headache, scalp tenderness and jaw claudication. Treatment is usually commenced immediately if the diagnosis is suspected as there is a risk of permanent visual loss due to ischaemia of the optic nerve, which is supplied by branches of the ophthalmic artery.

Trigeminal neuralgia affecting the mandibular or maxillary branches can cause severe pain or altered sensation over their anatomical distributions. Sinusitis can present with headache and pain over the cheeks, orbits or forehead and is common among patients of all age groups. Dental pain, due to a structural abnormality, such as a dental abscess, can also cause jaw pain and altered facial sensation.

Migraine headaches usually last for 4–72 hours but can persist for weeks in rare cases. Symptoms can include a severe, throbbing headache associated with sensitivity to light and sound, with nausea or vomiting. Migraines tend to affect women more frequently than men



and it is uncommon to have the first presentation after the age of 50 years, making it an improbable diagnosis in this case.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient should be thoroughly assessed by an ophthalmologist to exclude giant cell arteritis. If there is any indication that this condition is present, high-dose corticosteroids should be administered and the vascular surgeons should be contacted to consider a temporal artery biopsy.

An erythrocyte sedimentation rate (ESR) should be measured, as this marker of inflammation is often particularly high in giant cell arteritis.

The patient should be offered analgesia – the class of drug will depend on the most likely diagnosis. Migraine headaches may benefit from non-steroidal anti-inflammatory drugs, such as ibuprofen, and a triptan, such as sumatriptan. Carbamazepine and amitriptyline may provide benefit in the management of trigeminal neuralgia.

CASE PROGRESSION

The patient was reviewed by the ophthalmology registrar who saw no evidence of temporal arteritis or other ocular pathology. A computed tomography (CT) head scan was unremarkable aside from soft tissue changes within the sphenoid sinus, likely representing sinusitis. His ESR level was raised at 100 mm/hr (normal range 2–10 mm/hr in males aged 50+), but this was attributed to the flare of his rheumatoid arthritis. An autoimmune screen was sent and the patient was diagnosed with a likely tension headache. He was given simple analgesia, which relieved his headache, and he was discharged home for outpatient follow-up in the rheumatology clinic.

He represented to hospital 2 weeks later with left-sided facial swelling, predominantly along the jaw line, with pain upon opening the jaw or clenching his teeth. He had been feeling generally unwell at home with weakness and nausea. He had been unable to walk upstairs at home and had been sleeping on the sofa. He visited his dentist who diagnosed a dental abscess and commenced metronidazole, although the dentist noted that examination was difficult as the patient could not open his mouth very wide. He had seen his general practitioner that morning who had advised that he return to hospital.

The patient appeared drowsy and lethargic but was haemodynamically stable. There was visible left-sided facial swelling, predominantly over the left submandibular arch. Blood tests showed that the creatinine level had risen to 277 $\mu\text{mol/L}$. Intravenous co-amoxiclav was commenced for presumed sepsis secondary to a dental abscess. He was started on intravenous fluids in the evening and became confused overnight. A corrected calcium level was added onto his bloods from the day before and was found to be markedly elevated at 4.1 mmol/L (reference range 2.20–2.60 mmol/L).

A magnetic resonance imaging (MRI) scan of the head and neck showed multifocal bony disease involving the calvarium, skull base, facial bones and cervical vertebrae with extension of the left mandibular and left sphenoid lesions and some dural involvement along the floor of the middle cranial fossa (see [Figure 88.1](#)). Appearances were reported to be consistent with a multifocal aggressive process, favouring metastatic disease. The impression was that the patient's lung cancer may have recurred and that head and neck metastases were now present.

The hypercalcaemia was treated with aggressive fluid rehydration and intravenous pamidronate. A CT positron emission tomography (PET) scan showed extensive bony lytic

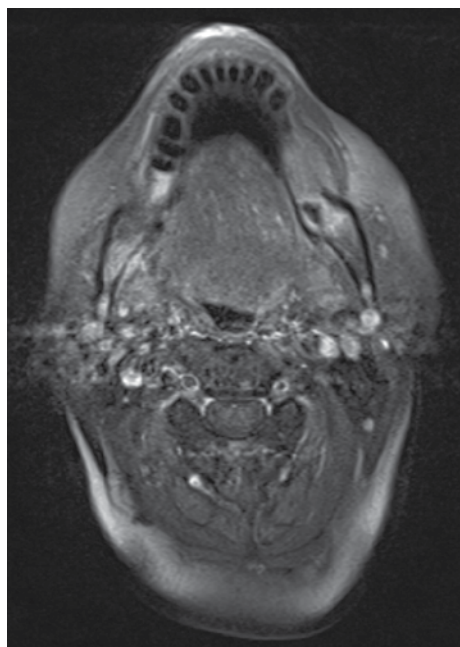


Figure 88.1 MRI scan of the head and neck.

destruction. A bone marrow aspiration and trephine was performed and the appearances were consistent with plasma cell myeloma.

Final diagnosis: Plasma cell myeloma with head and neck lesions.

OUTCOME

The patient's hypercalcaemia resolved and he felt symptomatically much improved. He commenced Velcade-thalidomide-dexamethasone chemotherapy and remains under the care of the haematology team. When the initial CT head scan was re-reviewed, in view of the MRI findings, the lytic lesions were apparent.

CASE DISCUSSION

Hypercalcaemia often presents with aches and pains, nausea and confusion. In this case, hypercalcaemia developed due to breakdown of bone in the context of malignant infiltration. The patient also had an acute kidney injury, which may have been due to nephrocalcinosis, or high levels of monoclonal urinary immunoglobulin light chains (Bence Jones proteins) causing nephropathy. Amyloidosis is also associated with multiple myeloma and may lead to renal impairment.

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CASE 89: HAEMOPTYSIS AND DIPLOPIA

PATIENT HISTORY

A 24-year-old woman presented to the emergency department complaining of a 2-week history of nausea, vomiting and shortness of breath on exertion. She also reported a 1-week history of cough productive of blood-stained sputum. When asked about her general health, she described episodes of diplopia that were becoming increasingly frequent and an intermittent sensation of chest discomfort ('heaviness or pressure on my chest') that was worse at night. She denied experiencing weight loss or fevers. She had no past medical history and her only medication was the combined oral contraceptive pill. She worked as a data analyst and lived with her parents. She had never smoked, drank around 5 units of alcohol per week and denied recreational drug use. She had only travelled to Italy in childhood.

EXAMINATION

Initial observations: T 37.0°C, HR 70 bpm, BP 130/80 mm Hg, RR 18, SpO₂ 100% on room air.

The patient appeared clinically well. Her chest was clear to auscultation and her heart sounds were normal. Her abdomen was soft and non-tender. There was no cervical or axillary lymphadenopathy present (inguinal lymphadenopathy was not assessed) and there was no oral candidiasis present. Neurological examination, including assessment of cranial nerves II, III, IV and VI, was unremarkable.

INITIAL RESULTS

Routine blood tests: WCC 9.1, Hb 122, Plt 378, Na 140, K 4.4, Creat 62.

Chest x-ray: The left hilum is filled with an approximately 20 × 15 mm opacity suspicious for a mass (see [Figure 89.1](#), arrow points to lesion; also note tracheal deviation).

DIFFERENTIAL DIAGNOSES

The patient presents with a constellation of symptoms including haemoptysis, dyspnoea, chest pain, vomiting and diplopia. Her chest x-ray shows a probable mass around the left hilar region which is causing deviation of the trachea and left main bronchus. For a patient in their 20s, there should be a high index of suspicion for Hodgkin's lymphoma.

A thymoma typically presents with symptoms of mass compression, such as chest discomfort or shortness of breath. Around 40% of patients will have features of myasthenia gravis, such as ptosis, diplopia or fatigable skeletal muscle weakness.

Tuberculosis is another possible diagnosis and a relatively common cause of hilar enlargement and upper lobe mass formation. Primary infection is usually seen on a chest x-ray as patchy or lobar consolidation, but cavitation or large tuberculoma formation may also occur.

Primary lung cancer is very uncommon in patients of this age group but nevertheless should be excluded. The ocular symptoms may form part of an associated paraneoplastic syndrome.

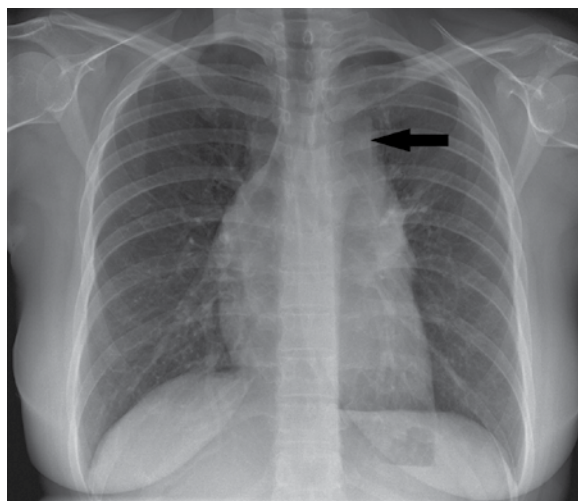


Figure 89.1 Chest x-ray showing left hilar mass.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient does not have large volume haemoptysis and sounds clinically well so she does not necessarily need to be admitted provided further investigations can be performed over the next few days.

She will require a computed tomography (CT) scan of her chest, abdomen and pelvis to characterise the mass and identify whether there are other masses present or if there is significant lymphadenopathy (which may be amenable to biopsy).

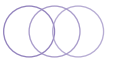
If a mass is confirmed a tissue sample will be required to enable histological diagnosis. A biopsy of the mass may be possible via a CT-guided procedure and this should therefore be discussed with the interventional radiology team. Serology for acetylcholine receptor auto-antibodies can also be sent if myasthenia gravis is considered a possible diagnosis.

CASE PROGRESSION

The emergency department arranged a CT scan of the patient's chest, abdomen and pelvis, to take place the following morning. This showed no abnormalities aside from the known mass. A CT-guided biopsy was performed.

The patient was re-examined, specifically looking for signs of myasthenia gravis. Fatigable ocular weakness was identified when the patient was asked to look upward for 30 seconds. She also had upper limb fatigability. The biopsy results showed thymic epithelial cells consistent with a thymoma.

Final diagnosis: Thymoma.



OUTCOME

The patient underwent a surgical resection of the thymoma 2 weeks later.

CASE DISCUSSION

This patient presented with symptoms of mass compression as well as the autoimmune condition, myasthenia gravis, which represents a paraneoplastic phenomenon in this situation. This is a neuromuscular disorder that is thought to occur following the development of autoantibodies against post-synaptic nicotinic acetylcholine receptors. A proportion of patients who have symptoms of myasthenia gravis but no detectable autoantibodies against the acetylcholine receptors will instead have antibodies against the muscle-specific receptor tyrosine kinase (MuSK).

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CASE 90: LOSS OF VISION AND OPHTHALMITIS

PATIENT HISTORY

A 30-year-old woman was referred from a specialist eye unit to the emergency department as the ophthalmologist who assessed her suspected that she may have septic arthritis. The referral letter stated that 1 month prior to this, the patient had become unwell with coryzal symptoms followed by a persistent sore throat, fever and feeling of general malaise. Several days later, she noticed that her right eye had become red and tender and that her vision in this eye was slightly blurred. She attended the eye unit and was treated with topical corticosteroids. Over the past week she had developed arthralgia affecting her knees and hips. Her left knee was swollen and hot to touch. She had no other past medical history and took no other medications. She worked as a florist and had not travelled abroad in recent years. The patient was to be admitted under the medical team with daily ophthalmology input.

EXAMINATION

Initial observations: T 37.2°C, HR 90 bpm, BP 116/72 mm Hg, RR 14, SpO₂ 99% on room air.

There was swelling over the left knee with a palpable effusion present. The knee was erythematous and hot to touch. Full range of movement was preserved, but her pain increased on flexion of the knee. The right knee was tender on palpation, but there was no visible joint abnormality. Bilateral hip pain was present without swelling or impaired range of movement; all other joints appeared normal.

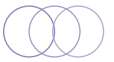
INITIAL INVESTIGATIONS

Routine blood tests: WCC 16.9, N^o 13.3, Hb 130, Plt 356, Na 138, K 4.0, Creat 66, CRP 53.

DIFFERENTIAL DIAGNOSES

The patient presents with a sore throat, eye pain and a possible septic arthritis of the knee. Septic arthritis of the left knee may have followed either a bacterial upper respiratory tract infection or a recent (unconnected) viral illness and is the main diagnosis to investigate and exclude at this stage.

Reactive arthritis (formerly Reiter's syndrome) can be triggered by infections, with common bacterial pathogens including *Chlamydia trachomatis* and *Salmonella* spp. Patients classically present with conjunctivitis, oligoarthritis and non-gonococcal urethritis – the patient should be specifically asked whether she has experienced dysuria. Disseminated *Neisseria gonorrhoeae* infection can present with conjunctivitis and arthralgia, and septic arthritis in severe cases.



Inflammatory arthritis, including psoriatic arthritis, presents with mono- or oligoarthritis, often on a background of psoriasis. Anterior uveitis is associated with inflammatory arthritis, and this may be the cause of the patient's red eye.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient should have an x-ray of the left knee, looking for erosions, loss of joint space and any evidence of fracture or joint displacement. Soft tissue swelling and joint effusion will also be observed.

If septic arthritis is thought to be likely, the patient's knee should be aspirated and intravenous antibiotics administered. The joint aspirate should be examined for the presence of pus cells or crystals and sent for bacterial culture. The rheumatology and/or orthopaedic team may need to be involved, depending on the underlying diagnosis.

CASE PROGRESSION

The orthopaedic team reviewed the patient in the emergency department and saw no evidence of septic arthritis. The left knee joint was aspirated and microscopy was unremarkable, with no crystals or pus cells seen and there were no organisms present on Gram stain. Magnetic resonance imaging (MRI) of the hips and pelvis showed high signal and enhancement of the right hip joint capsule with a 0.5 cm effusion. The rheumatology team felt that this was a reactive oligoarthritis.

Blood cultures did not isolate any organisms. HIV and syphilis serology were negative. *Neisseria gonorrhoea* and *Chlamydia trachomatis* infections were not detected on vaginal swabs or urine samples.

The hospital ophthalmology team continued topical steroids but noted that her vision had deteriorated rapidly over 48 hours, to the point where she could only perceive light and a right relative afferent pupillary defect was now present.

The patient complained of worsening pain in the right eye. The intra-ocular pressure was raised at 24 mm Hg compared with 13 mm Hg in the left eye (reference range: 10–21 mm Hg). Acetazolamide treatment was given for ocular hypertension.

Slit light examination identified corneal oedema and a 5 mm hypopyon in the anterior chamber. An ultrasound showed the presence of a retinal abscess. She underwent a vitreous aspirate, which showed no organisms on Gram stain. An intravitreal injection of vancomycin, amikacin and amphotericin was administered. The aspirate was cultured and *Neisseria meningitidis* (resistant to vancomycin but sensitive to amikacin) was isolated.

The patient underwent a vitrectomy, lensectomy and anterior-chamber wash-out. She received a further intravitreal injection of vancomycin, ceftazidime and amphotericin. Samples were taken to the microbiology laboratory where gram-positive cocci were seen on the Gram stain. *Neisseria meningitidis* was again isolated in the sample and polymerase chain reaction (PCR) testing confirmed the presence of this organism. Intravenous ceftriaxone was administered for 7 days.

Final diagnosis: Right endogenous endophthalmitis secondary to presumed transient *Neisseria meningitidis* bacteraemia, with reactive arthritis.



OUTCOME

The patient was discharged home with a further 3 weeks of oral antibiotic treatment. Her joint pain had resolved fully by this point and her inflammatory markers had normalised. It was hoped that once the post-infection inflammatory changes had resolved, the patient may be a suitable candidate for an intraocular lens implant. The eye remained persistently inflamed despite a course of dexamethasone eye drops and eventually became phthisical (shrunken and non-functional). The oculoplastics team performed an evisceration (removal of the intraocular contents) and reconstruction.

CASE DISCUSSION

Neisseria meningitidis (meningococcus) is a gram-negative bacterium that causes severe sepsis, with sequelae including meningitis and disseminated intravascular coagulation (DIC). In the United Kingdom, *Neisseria meningitidis* is a notifiable organism (causative agent) and Public Health England were informed. They have since initiated contact tracing.

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CASE 91: A HOLIDAY SOUVENIR

PATIENT HISTORY

A 45-year-old man was referred to the emergency department in early January by his general practitioner with a suspected pulmonary embolism. He described a 12-day history of fevers, rigors, night sweats, right-sided chest pain on deep inspiration and right-sided abdominal pain. Four days earlier, he had started a course of oseltamivir (for presumed influenza) and had been feeling nauseated with several episodes of vomiting since then. He had no past history, aside from an appendectomy in childhood, and took no regular medications.

Three weeks earlier, he had returned from a 9-month trip around the world, including Asia (Thailand, India, Vietnam and Malaysia: March–May), the Middle East (Bahrain and Qatar: June–July), Africa (Ghana, Kenya, Botswana and Namibia: August–September) and North America (United States and Canada: October–December). He had not taken malaria prophylaxis for the duration of the trip and was unsure if he had received travel vaccinations. He had drunk water from lakes and streams while in Canada. He had travelled with his wife, who was well. When in India, he experienced two diarrhoeal illnesses, but the trip was otherwise uneventful. He had previously worked as a banker but was not currently employed. He was an ex-smoker with a 10 pack year history and consumed around 8 units of alcohol per week.

EXAMINATION

Initial observations: T 38.9°C, HR 105 bpm, BP 155/65 mm Hg, RR 34, SpO₂ 99% on room air.

Systems examination was significant for pain in the right upper quadrant and right lumbar regions of the abdomen with voluntary guarding present. The examining doctor stated that they were unable to assess for organomegaly due to discomfort on deep palpation. Bowel sounds were normal and rebound tenderness was not present.

INITIAL INVESTIGATIONS

Routine blood tests: WCC 38.5, N^o 29.6, Hb 126, Plt 396, Na 127, K 4.5, Urea 3.8, Creat 58, Bili 28, Alb 34, ALT 51, ALP 336, GGT 270, Amylase 55, CRP 413.

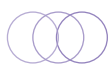
Chest x-ray: lung fields were clear, but there was elevation of the right hemidiaphragm.

Urine dip: no positive findings.

DIFFERENTIAL DIAGNOSES

The patient has an extensive travel history and now presents with fevers and right-sided chest and abdominal pain. He has markedly elevated inflammatory markers and an elevated right hemidiaphragm, which could indicate that phrenic nerve damage or hepatomegaly is present.

Schistosomiasis, a helminth infection caused by parasitic flatworms, presents with fever and abdominal pain, and patients may go on to develop hepatosplenomegaly. It is unclear whether the patient had fresh water exposure (aside from in Canada).



Giardiasis is a protozoal infection that is typically acquired from contaminated water. The disease is prevalent throughout the world. Symptoms include nausea, vomiting, diarrhoea, bloating and abdominal cramping.

Amoebiasis is caused by *Entamoeba histolytica* infection, which is transmitted via the faecal-oral route throughout most tropical areas. Gastrointestinal infections can result in bloody diarrhoea and around one in five people will develop hepatic abscesses.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

Blood and stool cultures should be taken, and stool should also be sent for ova, cysts and parasite assessment. Intravenous fluids should be given and his fluid balance should be monitored.

Intravenous paracetamol can be given as an anti-pyretic agent and additional analgesia may also be required. An abdominal ultrasound should be performed and the surgical team will need to review the patient if an acute abdomen is suspected.

Malaria films should be sent and the infectious diseases team will need to provide further advice regarding appropriate investigations in view of the patient's travel history.

CASE PROGRESSION

Intravenous fluids were given and the patient's tachycardia resolved and his fever settled. The infectious disease team reviewed the patient and advised taking at least three sets of blood cultures, sending malaria films and arranging an abdominal ultrasound scan. Antibiotics were not commenced, although the plan was to give co-amoxiclav and doxycycline if the patient deteriorated. His recent episodes of vomiting were attributed to side effects of oseltamivir.

He continued to develop intermittent fevers over the next 24 hours. No malaria parasites were seen on repeated blood films. An HIV test was negative. An abdominal x-ray showed no signs of bowel obstruction; however, hepatomegaly was incidentally observed ([Figure 91.1](#)). An abdominal ultrasound scan revealed two large focal masses within the liver ([Figure 91.2](#)), with the largest one being partially liquefied.

Three days later, the patient remained febrile but otherwise well. The largest liver mass was drained under ultrasound guidance and 400 mL dark fluid was collected in the first 24 hours. Immediately post-drain insertion, the patient improved clinically and inflammatory markers fell. Fluid cultures were negative and amoebiasis serology was positive (tires 1 in 640).

Final diagnosis: Amoebic liver abscess.

OUTCOME

The patient recovered fully and was discharged home to complete oral antibiotic therapy.

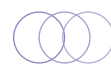


Figure 91.1 Abdominal x-ray showing an incidental finding of hepatomegaly.

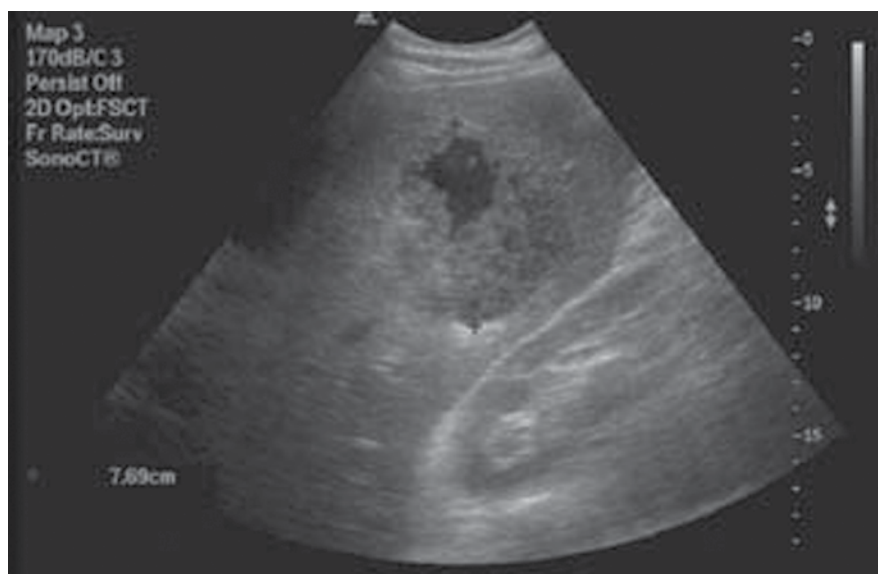


Figure 91.2 Abdominal ultrasound scan showing liver lesion.



CASE DISCUSSION

This patient had classic symptoms and signs of a liver abscess. In the United Kingdom, liver abscesses are most often due to infections, such as appendicitis and diverticulitis. In someone with an appropriate travel history, amoebic liver abscesses must be considered.

Over 10% of the world's population is infected with *Entamoeba histolytica*. A stool assessment (ova, cysts and parasites) or an *E. histolytica* faecal antigen assay are appropriate investigations in the context of gastrointestinal symptoms, but when additional sites are effected, amoebic serology tests should be carried out.

The definitive treatment for an amoebic liver abscess is drainage, covered with a course of antibiotics, such as metronidazole, which acts as a tissue amoebicide. The majority of amoebae in a host will remain in the intestine, so a luminal amoebicide, such as diloxanide or paromomycin, may also be given to prevent reinfection from the colon.

With thanks to Dr Pippa Newton and Dr Anna Goodman for their assistance with this case.

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CASE 92: A FEBRILE CANOEIST

PATIENT HISTORY

A 27-year-old man presented to the emergency department complaining of a 5-day history of fevers and myalgia. He described profound lethargy, feeling unable to get out of bed, for the preceding 24 hours and had experienced several episodes of diarrhoea and vomiting. He had developed a headache and photophobia earlier that morning and thought that his urine looked much darker than it usually did. He had delayed presenting to hospital as he stated that he had recently had unprotected sexual intercourse (UPSI) and was concerned that he may be told that he had contracted HIV. His past medical history included childhood measles. He took no regular medications. He worked as a canoe instructor and lived alone. He did not drink alcohol and had never smoked. He had not travelled outside of the United Kingdom for at least 2 years.

EXAMINATION

Initial observations: T 38.4°C, HR 98 bpm, BP 114/74 mm Hg, RR 14, SpO₂ 98% on room air.

The patient was visibly jaundiced and looked unwell. His chest was clear and cardiovascular examination was unremarkable. His abdomen was diffusely tender with voluntary guarding throughout. Bowel sounds were quiet. There was no rebound tenderness. There were no stigmata of chronic liver disease. Neurological examination was unremarkable with no objective signs of photophobia present.

INITIAL RESULTS

Routine blood tests: WCC 15.1, N^o 10.8, Hb 151, Plt 409, Na 134, K 3.1, Creat 106, Bili 58, ALT 81, ALP 74, CRP 214.

Venous blood gas: pH 7.32, lactate 2.8.

DIFFERENTIAL DIAGNOSES

The patient presents with jaundice preceded by a 5-day history of flu-like symptoms. He is a canoe instructor so leptospirosis needs to be at the top of the list of differential diagnoses. Other possibilities include viral infections, such as influenza, Epstein–Barr virus (EBV), cytomegalovirus (CMV), hepatitis (A, B, C and E), hantavirus (in view of possible exposure to rodents) and adenovirus, which may present with fevers.

In view of his UPSI, HIV seroconversion, syphilis, chlamydia and gonorrhoea infection all need to be considered.

Cholecystitis and pancreatitis are also common causes of jaundice and fever.



HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

Respiratory viral swabs should be taken, along with blood, urine and stool cultures and urine for leptospira polymerase chain reaction (PCR). Intravenous fluids, e.g. 1 L of 0.9% sodium chloride with 40 mmol potassium chloride, need to be prescribed and levels of electrolytes (corrected calcium, magnesium and phosphate) should be measured and replaced as necessary. Broad-spectrum antibiotics should be administered to treat possible hepatobiliary sepsis and leptospirosis infection (which would be covered by penicillin or ceftriaxone).

An amylase level should be checked to support or exclude a diagnosis of pancreatitis and an abdominal ultrasound scan should be requested. An INR level should be taken to assess the hepatic production of clotting factors. Serology for hepatitis A, B, C and E should be sent, as well as EBV, CMV and HIV.

CASE PROGRESSION

The patient was admitted under the medical team with presumed viral hepatitis. An abdominal ultrasound scan was attempted but, even with analgesia, the patient was unable to tolerate the procedure.

A computed tomography (CT) scan of his abdomen was performed, showing mild cholecystitis with periportal oedema and minor gallbladder thickening. He continued to have fevers of 38°C and his inflammatory markers remained elevated. A viral hepatitis screen did not identify a viral cause of the patient's symptoms.

The infectious diseases team reviewed the patient and, upon hearing that his occupation involved frequent contact with canals and rivers, sent urine and serum samples to test for leptospirosis and hantavirus. Once the acute phase had been treated with ceftriaxone, a course of oral doxycycline was prescribed and the patient improved over the next 2–3 days. His fevers settled and his inflammatory markers began to decline. The jaundice resolved completely and his liver function tests normalised. A clinical diagnosis of leptospirosis was made.

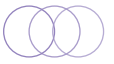
Final diagnosis: Leptospirosis.

OUTCOME

Blood samples tested for leptospirosis IgM were positive and the diagnosis was confirmed using PCR analysis of urine. A repeat sample was sent following an outpatient clinic appointment 3 weeks later, and the rise in serology titres seen was confirmative of a diagnosis of leptospirosis.

CASE DISCUSSION

Leptospirosis, also known as Weil's disease, is a bacterial infection that is contracted following exposure to bodily fluids of an infected animal. Farm animals, rodents and dogs are potential carriers of *Leptospira* sp. Occupational exposure can occur in farm and abattoir



workers, vets and people who are exposed to contaminated water, as in this case. Patients typically present with flu-like symptoms, but meningoencephalitis, hepatitis and renal failure may develop in severe infections.

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CASE 93: TACHYCARDIA LEADING TO VENTRICULAR FIBRILLATION

PATIENT HISTORY

A 47-year-old man attended the emergency department complaining of shortness of breath and palpitations. He had felt generally unwell over the preceding weeks, with a dry cough, dyspnoea, unintentional weight loss and fatigue. His past history included a resected gastric carcinoma (T4, N1, M0), and asthma, which had been present since childhood. He took 40 mg omeprazole OD and used a salbutamol inhaler several times daily. He had previously worked as a laboratory technician but was currently unemployed. He had no recent travel history. He was a current smoker with a 40 pack year history and did not drink alcohol.

EXAMINATION

Initial observations: T 37.5°C, HR 140 bpm, BP 120/68 mm Hg, RR 26, SpO₂ 92% on room air.

The patient appeared cachectic. Auscultation of the chest identified bi-basal crackles, consistent with pulmonary oedema. The patient was tachycardic with an irregularly irregular pulse.

INITIAL RESULTS

Routine blood results: WCC 5.0, Hb 120, Plt 131, Na 137, K 3.7, Creat 31 and CRP 46.

Electrocardiogram (ECG): atrial fibrillation with a rapid ventricular response rate (140–160 bpm).

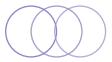
DIFFERENTIAL DIAGNOSES

The patient has presented with atrial fibrillation and probable pulmonary oedema. Coronary artery disease leading to myocardial ischaemia causes the development of both heart failure and cardiac arrhythmias. The onset of atrial fibrillation may precipitate heart failure, due to insufficient diastolic filling times and impaired atrial systole, leading to a reduced cardiac output.

Community-acquired pneumonia may be responsible for the cough and low-grade fever, and the infection may be driving the tachycardia and atrial fibrillation.

The patient has a past history of gastric carcinoma and a possible recurrence of this needs to be considered. He complained of unintentional weight loss and appears cachectic, which could be indicative of a malignant process. The patient has a 40 pack year smoking history and has a cough with dyspnoea, and lung cancer should therefore also be suspected.

A pulmonary embolism may be responsible for the tachycardia and low oxygen saturations. The patient has a history of malignancy, which puts him at increased risk of venous thromboembolism formation.



HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

Intravenous access should be established. A chest x-ray should be performed to confirm pulmonary oedema and identify possible consolidation or mass lesions. Intravenous furosemide boluses can be administered to treat the fluid overload while monitoring the patient's blood pressure.

A septic screen should be performed to identify a potential source of infection. Broad-spectrum antibiotics should be commenced. The patient's magnesium level must be checked and, if necessary, supplemented, targeting a level of 1.0–1.4 mmol/L (reference range 0.75–1.0 mmol/L), as hypomagnesa promotes arrhythmogenesis, and a higher level is preferable in patients with a high risk of arrhythmias. A thyrotropin (TSH) level should be checked, as hyperthyroidism is a common cause of tachycardia.

The tachycardia may resolve with fluids and antibiotics. Digoxin would be the drug of choice to control the ventricular rate as this patient has a history of asthma and therefore may not tolerate beta-blockers (although bronchospasm rarely occurs with β_1 -selective agents, such as bisoprolol and metoprolol).

CASE PROGRESSION

A chest x-ray was performed, showing bilateral pleural effusions with widespread pulmonary oedema consistent with cardiac failure (see [Figure 93.1](#)). The patient was admitted under the cardiology team, where intravenous boluses of furosemide were commenced for fluid overload. Intravenous co-amoxiclav was given for possible sepsis.

Twenty-four hours later, the patient remained tachycardic and oral digoxin was prescribed (with two loading doses) for control of his heart rate. On closer examination, he was noted

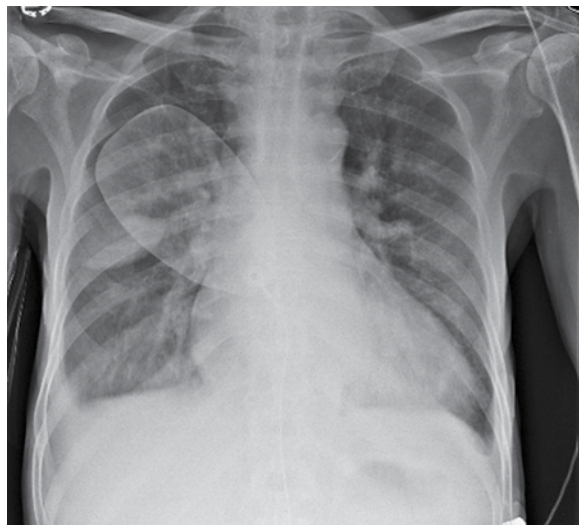


Figure 93.1 Chest x-ray showing pulmonary oedema and small bilateral pleural effusions. A defibrillator pad is present on the right chest wall.

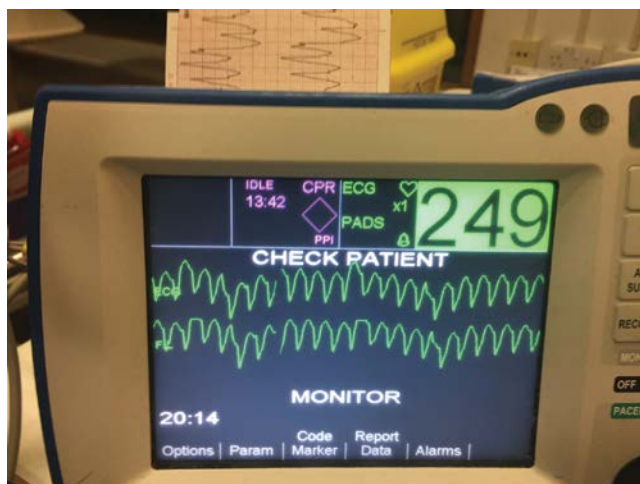


Figure 93.2 Ventricular tachycardia seen on the monitor of a defibrillator.

to have a visible goitre and exophthalmos. Thyroid function tests were sent. His heart rate remained at around 160 bpm. The following morning, he developed ventricular fibrillation that responded to defibrillation.

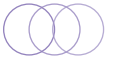
The patient's TSH level was phoned through to the ward as an urgent result during his resuscitation – TSH levels were undetectable (reference range 0.27–4.2 mIU/L) and free T3 was >100 pmol/L (reference range 3.1–6.8 pmol/L). He remained in atrial fibrillation with a rate of 150–160 bpm. Regular bisoprolol was started and uptitrated to achieve control of the heart rate. The endocrine team commenced propylthiouracil, potassium iodide and hydrocortisone treatment. An anti-thyroglobulin antibody level was 1455 U/mL (reference range 0–150 U/mL).

ECGs post-cardiac arrest showed some anterior ST elevation and an echocardiogram showed severely impaired left ventricular (LV) function (ejection fraction 20%). Following intermittent runs of ventricular tachycardia, one of which required direct current cardioversion (see [Figure 93.2](#)), the patient underwent an angiogram and subsequently, an angioplasty. An implantable cardioverter defibrillator (ICD) was inserted and he was commenced on warfarin. A three-dimensional echocardiogram showed no evidence of dyssynchrony. His heart failure medications were optimised.

Final diagnosis: Thyrotoxicosis secondary to Graves' disease.

OUTCOME

The patient made a good recovery over the following weeks and was eventually discharged home. He will be followed up by the cardiologists to monitor his cardiac function and the endocrinologists who are likely to recommend that a surgical thyroidectomy be performed.



CASE DISCUSSION

Thyrotoxicosis classically presents with tachycardia, fatigue and weight loss, all of which were present in this patient. Graves' disease is an autoimmune condition whereby autoantibodies bind to the TSH receptor, leading to excessive secretion of free T3 and T4 and thyroid hyperplasia.

Definitive treatment options include radio-iodine therapy or surgical thyroidectomy. In this case, propylthiouracil was given – this drug inhibits thyroperoxidase activity and thus inhibits the production of thyroid hormones. Potassium iodine and a short course of corticosteroids were also given to reduce thyroid hormone levels. Surgery was scheduled for a later date.

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CASE 94: CONFUSION WITH MULTIPLE SWOLLEN JOINTS

PATIENT HISTORY

A 70-year-old man was brought to the emergency department after collapsing at the theatre. He described feeling weak over the hours leading up to his collapse. He was unsure if he had lost consciousness and was unable to describe the event in detail. He denied preceding palpitations or chest pain. He also relayed a history of around 10–15 episodes of diarrhoea over the preceding 48 hours but otherwise felt well. The diarrhoea was described as watery, brown stool with no blood or mucus present. His past medical history included aplastic anaemia and complete heart block, for which he had a pacemaker in situ, and a right-sided total knee replacement that had been performed 2 years earlier. His regular medications were ciclosporin, citalopram, diazepam, vitamin B₁₂ and folic acid (doses unknown). He was a retired irrigation engineer who lived with his wife and grandson.

EXAMINATION

Initial observations: T 38.1°C, HR 70 bpm, BP 130/80 mm Hg, RR 16, SpO₂ 98% on room air.

Multiple pigmented, pedunculated lesions were distributed across the patient's torso. The lesions were up to 60 mm in diameter (the patient's wife stated that they had been small, pale lesions around a year ago but over the past 6 weeks had become very large and dark). The examining doctor noted that the patient was reluctant to move his left shoulder and when he examined this, he found that the joint was swollen with a reduced range of movement – the patient and his wife explained that he had fallen onto that side. The patient had word-finding difficulties and was slightly confused, with an abbreviated mental test score (AMTS) of 8/10 (points lost for concentration and recall). His wife informed us that this was out of character for him and she felt he had been slightly confused over the preceding fortnight. Systems examination, including a full neurological assessment, was otherwise unremarkable.

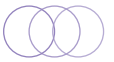
INITIAL INVESTIGATIONS

Routine blood results: WCC 5.6, N^o 4.0, L^o 0.8, Hb 93, MCV 109, Plt 26 (baseline 30–40), Na 133, K 4.4, Urea 11.7, Creat 100 (baseline 80), Bili 15, ALT 23, ALP 67, Alb 41, GGT 88, INR 1.1, CRP 207.

Chest x-ray: no pulmonary oedema, focal consolidation or mass lesions seen.

DIFFERENTIAL DIAGNOSES

The most likely cause for the patient's collapse is dehydration following a diarrhoeal illness. In view of his immunosuppression with ciclosporin, sepsis should be considered and treated early as the presentation may be atypical.



With regard to the underlying pathology, gastroenteritis is a possible diagnosis, particularly in view of his history of aplastic anaemia, which leads to an increased risk of infections due to chronic neutropenia. Indeed, this patient has a C-reactive protein (CRP) level of 207 mg/L without an elevated white cell count (WCC), perhaps indicating that he is unable to mount an appropriate leucocytosis in response to inflammatory stimuli. Alternatively, if his baseline WCC is significantly lower than this, he may have mounted a relative leucocytosis. All infective causes of diarrhoea should be considered, such as *Campylobacter jejuni*, which may disseminate in those with immunosuppression.

Diverticulitis is a common cause of fever and diarrhoea in older patients. The initial presentation of inflammatory bowel disease has a bimodal distribution, with a large peak in the second and third decades of life, followed by a smaller peak in patients aged 60 years, and this event could represent a flare of underlying Crohn's disease or ulcerative colitis.

Malignancy, such as cutaneous lymphoma, is an important diagnosis to exclude. Immunosuppression is associated with an increased risk of neoplasm formation. Other possible malignancies include bowel cancer, as well as carcinoid disease, which classically presents with diarrhoea and is associated with cutaneous metastases.

Sepsis is in the list of differential diagnoses and possible sources would include the gut (as above) or a urinary tract infection. He has both a pacemaker and a total knee replacement in situ and any organism may therefore disseminate to these foreign bodies. The pain in his left shoulder raises the possibility of this location of infection in a native joint.

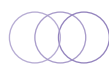
Pseudomonas infection can disseminate in skin in immunosuppressed patients, but the lesions are not typical for ecthyma gangrenosum in view of their prolonged presence.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient will require a full septic screen including blood, stool, cerebrospinal fluid (CSF) and urine cultures and broad-spectrum antibiotics and aggressive rehydration will need to be given immediately and should not be delayed while waiting for a lumbar puncture. X-rays of the patient's chest (to look for signs of infection) and his left shoulder (to identify fractures or joint displacement) should be requested. A computed tomography (CT) head scan should be performed to look for signs of subdural haemorrhage, in view of the patient's confusion on a background of thrombocytopenia and a recent fall. Magnetic resonance imaging (MRI) scans of the shoulder and knee would be helpful but in view of his pacemaker a positron emission tomography (PET) CT may be a more appropriate investigation and is helpful in the diagnosis of possible prosthetic infections.

CASE PROGRESSION

The patient was admitted under the haematology team, who prescribed broad-spectrum antibiotics and intravenous fluids. An x-ray of the left shoulder was unremarkable, with no evidence of fracture or joint displacement. His diarrhoea settled but he became increasingly confused over the next 12 hours. A CT head scan was unremarkable. The team planned to perform a lumbar puncture to investigate for possible encephalitis, but the patient developed worsening agitation and did not tolerate the procedure. An MRI scan of the brain was



requested but the radiology team explained that the patient's pacemaker was a relative contraindication to this investigation.

The patient was consistently febrile, at 38–39°C. His Hb level fell to 75 g/L over a course of 2 days, possibly partly due to ongoing intravenous fluid administration. His shoulder remained tender. The orthopaedic team reviewed the patient and was concerned that he may have developed septic arthritis. They went on to aspirate frank pus from the joint. Calcium pyrophosphate crystals were also observed in the joint aspirate. The orthopaedic team noted erythema and swelling around the right knee, although they were unable to aspirate fluid. The antibiotic regime was modified to treat presumed septic arthritis.

On day 4 of admission, the patient developed neutropenia and his sepsis worsened. He underwent a washout of the knee joint, which found blood-stained fluid with no pus. Fluid cultures from the left shoulder grew *Streptococcus agalactiae* (group B streptococcus). The dermatology team reviewed the skin lesions and diagnosed multiple squamous cell carcinomas, which may be secondary to ciclosporin-related immunosuppression.

The patient's inflammatory markers improved but he remained confused. On day 8 of the admission, a lumbar puncture was performed (a pool of platelets was transfused before the procedure) with no CSF abnormalities identified. An electroencephalogram (EEG) showed encephalopathic changes, possibly due to ongoing infection. On day 10, the infectious diseases registrar re-examined the patient and noted a new pansystolic murmur and splinter haemorrhages. A urine dip found microscopic haematuria. A transoesophageal echocardiogram identified a vegetation on the pacing lead. His left elbow was now hot and swollen and his right knee was erythematous once again. Both joints were aspirated, revealing blood and pus.

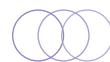
Final diagnosis: Disseminated *Streptococcus agalactiae* (group B streptococcus) with endocarditis, native joint septic arthritis and prosthetic joint infection in an immunosuppressed patient.

OUTCOME

The patient underwent a removal of his right-sided total knee replacement prosthesis and was scheduled to undergo a pacemaker explantation but he deteriorated and became unresponsive with loss of cardiac output requiring cardiopulmonary resuscitation with defibrillation. He had a protracted stay on the intensive treatment unit with multiple courses of antibiotics but was eventually well enough to step down to ward-based care. He is currently undergoing rehabilitation.

CASE DISCUSSION

Immunosuppression increases the risk of sepsis and disseminated fungal infections. Presentation may be atypical in view of immunosuppression and the inability to mount an appropriate immune response may lead to an absence of typical signs such as fever. The presence of skin lesions in an immunosuppressed patient should lead to suspicion of dissemination of bacteria to skin, as occurs in meningococcal sepsis and ecthyma gangrenosum. Blood cultures will commonly reveal the cause in such cases.



When found in blood, the presence of *Streptococcus agalactiae* (group B streptococcus) suggests a deep-seated infection is present. In neonates it may cause sepsis or meningitis. In an elderly man possible sources might be pneumonia, endocarditis, arthritis, osteomyelitis or prostatitis and a transoesophageal echocardiogram, chest x-ray, joint and prostate examination should always be performed when this organism is found. In the presence of foreign bodies these should be presumed to be infected and investigations should be performed accordingly.

This patient developed a native joint septic arthritis associated with bacterial seeding on a pacemaker lead, on which a vegetation was observed. Treatment of an infected pacemaker site usually requires explantation of the device followed by a course of antibiotics and subsequent implantation of a new device. In patients where this is not possible, due to frailty or extremes of age, long-term palliative antibiotics may be required.

In the United Kingdom, the organism remains susceptible to penicillins and treatment with broad-spectrum antibiotics can be narrowed once the infection is identified.

With thanks to Dr Anna Goodman for her help with this case.

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CASE 95: A CONFUSED YOUNG PERSON WITH FOCAL NEUROLOGICAL SIGNS

PATIENT HISTORY

A 26-year-old woman was brought to the emergency department by her father who reported that he had found her confused and incoherent in her flat. She had been acting 'out of character' over recent weeks, demonstrating reluctance to leave her house and complaining of a headache. She had telephoned her father to tell him that she had been vomiting for several hours. She had been incontinent of urine and faeces. The patient was unable to give any further history. Her past medical history was significant for bipolar disorder for which she received monthly depot injections of zuclopenthixol. She took no other drugs, did not drink alcohol and was a non-smoker.

EXAMINATION

Initial observations: T 38°C, HR 54 bpm, BP 160/96 mm Hg, RR 15, SpO₂ 94% on room air.

The patient was disorientated and became agitated during the examination. Her chest was clear and her heart sounds were normal. Her abdomen was soft and non-tender. A digital rectal examination found faecal impaction with overflow diarrhoea. Her pupils appeared dilated (5–6 mm) and reacted sluggishly to light. She had increased tone throughout all limbs, 6 beats of clonus were noted bilaterally and her plantars were upgoing. Neither neck stiffness nor photophobia was observed. Fundoscopy revealed blurred disc margins. Oral and vaginal candidiasis were present.

INITIAL INVESTIGATIONS

Routine blood results: WCC 12.0, N^o 10.6, Hb 118, MCV 102, Plt 265, Na 137, K 4.6, Urea 3.8, Creat 39, CRP 62.

Electrocardiogram (ECG): see [Figure 95.1](#), normal sinus rhythm with deep S waves in lead I, in addition to Q and T waves in lead III.

Chest x-ray: patchy right basal atelectasis.

DIFFERENTIAL DIAGNOSES

The patient presents with altered mental state, fever and neurological findings consistent with raised intracranial pressure (ICP) (dilated pupils, blurred optic disc margins) on a background of bipolar affective disorder and use of a typical anti-psychotic.

A space-occupying lesion, such as a subdural haematoma, intracerebral cerebral bleed or a malignant lesion may be responsible for her recent deterioration in mental state and the focal neurological signs. The patient has a candidiasis infection, which could be due to immunosuppression. If this were the case, she would be at increased risk of additional cerebral pathology, including a cerebral abscess, toxoplasmosis and cerebral tuberculosis.

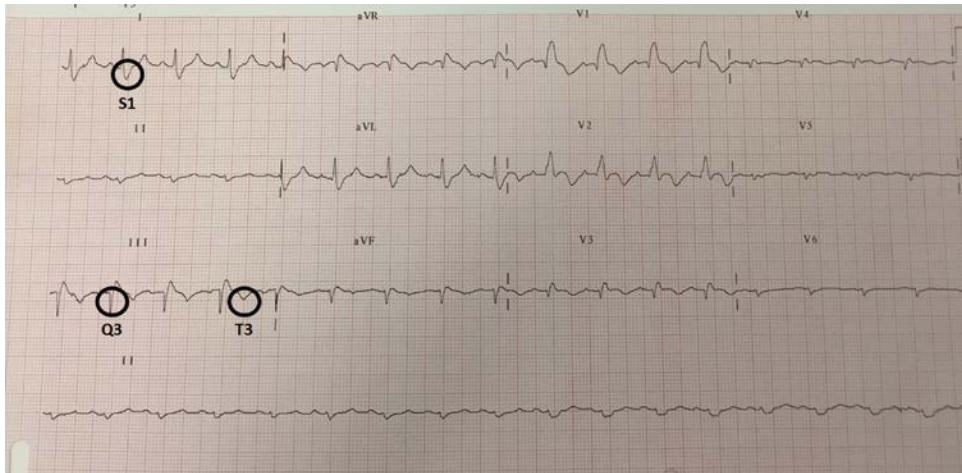
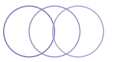


Figure 95.1 An ECG showing normal sinus rhythm with deep S waves in lead I, and Q and T waves in lead III.

Meningitis and encephalitis (particularly cryptococcal meningitis) may also explain the observed symptoms and signs.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

A computed tomography (CT) head scan should be performed to identify potential acute pathology. With clear signs of raised ICP, a lumbar puncture is unlikely to be performed acutely as there is a risk of trans-tentorial or uncal herniation. Empirical aciclovir and ceftriaxone should be given to treat presumed meningo-encephalitis.

The patient has reduced oxygen saturations and an arterial blood gas should therefore be performed to assess the gas exchange and acid-base status. Her ECG shows the 'S1Q3T3' pattern, which is classically associated with pulmonary embolism and a ventilation/perfusion (V/Q) scan should be considered.

CASE PROGRESSION

The patient was disorientated but retained capacity to decline treatment. She did not wish to have a CT scan of her brain and was therefore given empirical aciclovir and antibiotic therapy to cover potential meningoencephalitis and/or community-acquired pneumonia.

The patient became increasingly confused and agitated over the next 6 hours and lost capacity to decline lifesaving care. Repeat blood tests showed that her inflammatory markers had risen, with a white cell count (WCC) of 21.3×10^9 and C-reactive protein (CRP) of 188 mg/L. Her oxygen saturations fell to 74% on room air. An arterial blood gas on room air showed respiratory failure (pH 7.46, pCO₂ 5.37, pO₂ 5.8, BE +3.9, lactate 0.6).

Due to her worsening agitation and likelihood of catastrophic deterioration without further management, the patient was intubated and mechanically ventilated. A CT head scan showed a superior sagittal sinus thrombosis (Figure 95.2a, arrow highlights the lesion), which

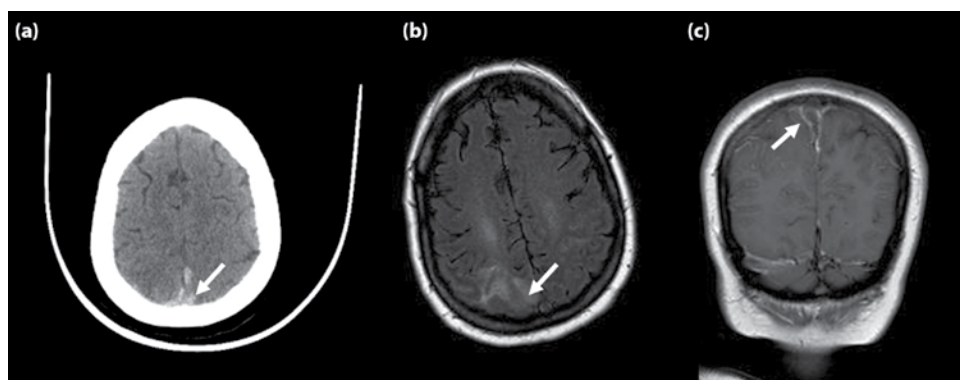


Figure 95.2 (a) CT image of the superior sagittal sinus thrombosis; (b and c) are MRI views of the lesion.

was confirmed with magnetic resonance angiography (MRA) imaging along with additional right transverse sinus thrombosis (Figure 95.2b, arrow highlights the lesion; Figure 95.2c, arrow points to the superior sagittal thrombus: opaque area outlined by contrast in white).

A CT pulmonary angiogram identified multiple large pulmonary emboli. The patient was anti-coagulated with low molecular weight heparin (enoxaparin, dosed at 1.5 mg/kg body weight). Several days later, the platelet count fell to 105×10^9 and it was thought that she had developed heparin-induced thrombocytopenia (HIT), which was subsequently confirmed with antibody testing. Enoxaparin was switched to fondaparinux (see Figure 95.3). Autoimmune testing was performed and lupus anti-coagulant was detected (strongly positive). A presumed diagnosis of anti-phospholipid syndrome was made.

Final diagnosis: Anti-phospholipid syndrome with heparin-induced thrombocytopenia.

OUTCOME

The patient developed a ventilator-associated pneumonia and moderate critical care myopathy. She had a protracted stay on the intensive treatment unit and required intense physical therapy and rehabilitation. Further outpatient autoimmune testing confirmed the diagnosis of anti-phospholipid syndrome. The patient will continue on lifelong anti-coagulation therapy.

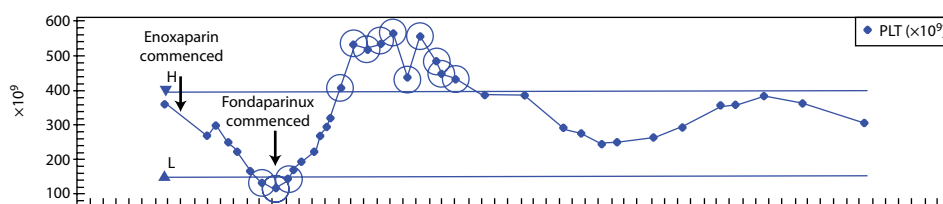
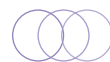


Figure 95.3 Platelet levels from admission until discharge.



CASE DISCUSSION

This patient was eventually diagnosed with anti-phospholipid syndrome. The revised classification criteria for anti-phospholipid syndrome include a history of vascular thrombosis and/or pregnancy morbidity (unexplained death of a morphologically normal fetus at 10 or more weeks of gestation, premature birth of a morphologically normal fetus due to eclampsia, pre-eclampsia or placental insufficiency, or three or more unexplained consecutive spontaneous abortions with parental chromosomal causes excluded), in addition to positive serology (lupus anticoagulant, anticardiolipin antibody, or anti- β 2 glycoprotein-I antibody) measured on at least two occasions, 12 weeks apart.

HIT is the development of thrombocytopenia following treatment with heparin and typically presents 4–10 days after treatment commences. It is much more common with unfractionated heparin and only rarely described with low molecular weight heparin, usually when there has been prior exposure to unfractionated heparin. Despite the low platelet count, patients are at high risk of thrombosis rather than bleeding. Type 1 HIT occurs following a direct effect of heparin on platelet activation and is not immune-mediated. Type 2 HIT is an immune-mediated phenomenon whereby patients develop antibodies to ‘platelet factor 4/heparin’ complexes leading to increased platelet activation and aggregation. Fondaparinux is commonly used to anticoagulate patients who have developed HIT as it has a comparatively low affinity for platelet factor 4.

With thanks to Dr Adam Nabeebaccus for his assistance with the case.

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CASE 96: DIARRHOEA AND PROXIMAL WEAKNESS

PATIENT HISTORY

A 40-year-old man presented to the emergency department following a collapse at home. He had a 4-day history of cramping abdominal pain and severe diarrhoea, opening his bowels 20–30 times per day and passing watery stool without blood or mucus. He had eaten at a Chinese restaurant several hours prior to his diarrhoea commencing, but the people he dined and shared food with were all well. He denied symptoms of fevers, cough or recent weight loss. He described passing reduced volumes of urine over the preceding 3 days, culminating in no urine output in the last 12 hours. His past medical history included a longstanding anaemia of unknown cause. He took no regular medications and was allergic to penicillin (unknown reaction). He lived alone and worked as a barrister. He denied both smoking and drinking excess alcohol, and did not use recreational drugs. He informed the team that he was penicillin-allergic. He stated that he had multiple male and female sexual partners most weekends and always used barrier contraception. He led an active lifestyle, taking part in a kickboxing class twice weekly and had last travelled abroad 3 months earlier when he visited Canada.

EXAMINATION

Initial observations: T 37.2°C, HR 98 bpm, BP 122/80 mm Hg, RR 14, SpO₂ 99% on air.

The patient appeared clinically dehydrated. His abdomen was soft with mild tenderness in the left iliac fossa. The examination was otherwise unremarkable.

INITIAL RESULTS

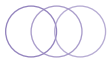
Routine blood results: WCC 20.3, N 18.1, Hb 119, MCV 77, Plt 126, Na 127, K 3.5, Urea 51.6, Creat 368, INR 1.4, CRP 364.

Chest x-ray: clear lung fields.

DIFFERENTIAL DIAGNOSES

The patient presents with a 4-day history of diarrhoea with raised inflammatory markers and a presumed severe acute kidney injury. Possible causative agents of the diarrhoea include *Campylobacter jejuni*, *Clostridium perfringens*, *Escherichia coli*, *Salmonella* spp., and *Shigella* spp. *Escherichia coli* O157:H7 is a particularly serious strain that can cause haemolytic-uraemic syndrome, where patients develop microangiopathic haemolytic anaemia, thrombocytopenia, renal failure and neurological sequelae. Shigellosis is now an increasingly prevalent sexually transmitted infection among gay and bisexual men in the United Kingdom.

Clostridium difficile colitis classically presents with a diarrhoeal illness and a profound leucocytosis. This infection is more common among patients who have had protracted or multiple courses of antibiotics – the patient should be specifically asked whether he has taken antibiotics recently.



The initial presentation of inflammatory bowel disease peaks in the second and third decades of life but remains a relatively common diagnosis among all age groups. The recent diarrhoeal illness could result from a flare of Crohn's disease or ulcerative colitis, particularly in view of the elevated white cell count (WCC) and C-reactive protein (CRP), which indicate that a severe inflammatory process has occurred.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient has a severe acute kidney injury. Intravenous fluids (e.g. 500 mL sodium compound lactate over 30 minutes) will need to be administered and you should reassess the patient's fluid status after this, before prescribing further fluids over the next few hours. A urinary catheter should be sited to ensure the recent anuria is not due to urinary retention and to allow accurate measurement of his urine output in response to fluids.

A venous blood gas can be taken to assess his acid–base status. A metabolic acidosis would be expected based on the degree of renal impairment that is present. The blood gas will also measure a lactate level, allowing an assessment of whether tissue hypoperfusion is present.

An abdominal x-ray should be performed, looking for dilated loops of large bowel (possible toxic megacolon), bowel wall oedema, bowel obstruction or imminent bowel wall perforation. If haemolytic-uraemic syndrome is suspected, a blood film should be sent to the laboratory to identify the presence of schistocytes (indicative of haemolysis).

Stool samples should be sent for culture (and in some laboratories will be processed rapidly for enteric polymerase chain reaction [PCR]) and to measure the level of faecal calprotectin, which is a marker of bowel inflammation. The gastroenterology team should be notified as they may consider performing a flexible sigmoidoscopy.

Rectal swabs for gonorrhoea and chlamydia should be taken as lymphogranuloma venereum presents with diarrhoea, as can rectal gonorrhoea. An HIV test should be performed.

CASE PROGRESSION

Intravenous fluids were given and a urinary catheter was sited. The patient passed 100 mL urine over the next hour. A blood film showed a leucocytosis, anaemia (no schistocytes were seen) and mild thrombocytopenia. The patient received a total of 8 L intravenous fluids over the next 24 hours. He maintained a good urine output and his diarrhoea began to settle. An autoimmune screen was sent as it was thought that a vasculitic process may be responsible for the patient's gastrointestinal symptoms and acute renal failure. He remained persistently febrile with his temperature varying between 38.5°C and 39.8°C.

By day 2 of his admission, his creatinine level had fallen to 190 µmol/L. Preliminary microbiology reports showed three of four blood culture bottles contained gram-positive cocci in chains. The patient complained of a dry cough and his oxygen saturations fell to 92% on room air. His diarrhoea had largely resolved, but he developed bilateral leg pain and, when he was examined, there was reduced power (4/5) at hip flexion and hip extension. His thighs and calves were tender when the muscles were palpated. The differential diagnosis now included invasive group A streptococcal infection causing pyomyositis, Guillain–Barré syndrome and myopathy. The infectious diseases team added clindamycin to the antibiotic regime. His creatine kinase (CK) level was within the normal range.

On day 5 of the admission, the patient's renal function had normalised and the blood cultures had grown *Streptococcus pyogenes* (group A streptococcus). Public Health England were notified, household contacts were provided with information about the condition and prophylaxis was prescribed where required. An HIV test was negative. A repeat chest x-ray showed right basal consolidation. The patient's symptoms of abdominal cramping and diarrhoea returned; he was now passing fresh blood in his stool. It was unclear whether this was related to his initial symptoms or whether the patient now had an antibiotic-related diarrhoea. His symptoms of leg weakness and myalgia worsened, with hip flexion and hip extension falling to 3/5 and knee flexion falling to 4/5 power bilaterally. The microbiology team felt that the lower limb symptoms could be due to underlying pyogenic myositis and advised allergy testing for penicillin, which proved to be negative and thus benzylpenicillin was commenced.

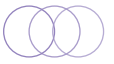
Hip x-rays were clear. A leg computed tomography (CT) showed localised fluid within the subcutaneous tissue indicative of localised inflammation. Flexible sigmoidoscopy and a CT scan of the chest, abdomen and pelvis were booked. The CT scan showed disseminated myositis and mediastinal lymphadenopathy. Bilateral pleural effusions developed.

Flexible sigmoidoscopy showed haemorrhagic proctitis (see [Figure 96.1](#)). The bloody diarrhoea continued, and the patient's haemoglobin level fell to 71 g/L. The presumed differential diagnosis now included ulcerative colitis and treatment was required in case of *C. difficile* infection. Metronidazole and mesalazine were commenced. Doxycycline was added in to cover possible lymphogranuloma venereum infection. The patient's bloody diarrhoea settled and he improved clinically. A leg magnetic resonance imaging (MRI) scan showed multiple tiny abscesses in the gluteal muscles running from the anorectum along the sciatic nerve.

Final diagnosis: Inflammatory bowel disease (IBD) with superimposed invasive group A streptococcal infection and development of pyogenic myositis, complicated by parapneumonic effusions and antibiotic colitis.



Figure 96.1 Flexible sigmoidoscopy image showing haemorrhagic proctitis.



OUTCOME

Histological results from biopsies taken during the flexible sigmoidoscopy were consistent with ulcerative colitis. The patient's renal function normalised and he was discharged home with analgesia and topical rectal steroids.

CASE DISCUSSION

Pyogenic myositis is an intramuscular infection, which develops following bacteraemia, usually in the context of pre-existing muscle trauma. In this case, the patient had (undiagnosed) underlying ulcerative colitis, which was thought to be responsible for his chronic anaemia. During a flare of ulcerative colitis, the patient developed a superimposed group A streptococcus infection resulting in bacteraemia and subsequent pyogenic myositis. The patient may have had a degree of pre-existing exercise-induced muscle damage due to his regular kickboxing classes.

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CASE 97: TB OR NOT TB?

PATIENT HISTORY

A 58-year-old woman presented to the emergency department complaining of fevers and haemoptysis. She had been feeling unwell for approximately 6 weeks, with general malaise, fatigue and unintentional weight loss. She described drenching night sweats for the past week. Her past medical history included hypercholesterolaemia, for which she took 40 mg atorvastatin OD. She was originally from Eastern India and had come to live in the United Kingdom 10 years earlier. She worked as a play therapist and lived with her husband, who was well. She had never smoked and did not drink alcohol.

EXAMINATION

Initial observations: T 38.2°C, HR 92 bpm, BP 132/86 mm Hg, RR 18, SpO₂ 96% on room air.

The patient appeared fatigued and had a body mass index (BMI) of approximately 17. Her chest had crackles at the right mid-zone and base. Cardiovascular examination was unremarkable. There was cervical lymphadenopathy, with two to three soft nodes of 10–15 mm present bilaterally.

INITIAL RESULTS

Routine blood results: WCC 14.5, N 11.8, Hb 118, Plt 290, Na 137, K 3.9, Creat 50, CRP 110.

Chest x-ray: clear lung fields, possibly some minor hilar lymphadenopathy bilaterally.

DIFFERENTIAL DIAGNOSES

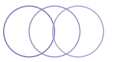
The patient presents with fevers, weight loss, night sweats and lymphadenopathy. Pulmonary tuberculosis is the most probable diagnosis, particularly as the patient has spent most of her life in an area where tuberculosis is endemic.

Lymphoma is also a likely diagnosis and a lymph node biopsy will need to be performed to exclude this. Other malignancies, including primary lung cancer or breast cancer with lung metastases, should be considered.

Pulmonary sarcoidosis typically presents with a dry cough and dyspnoea. Hilar lymphadenopathy may be present on a chest x-ray. Uveitis and erythema nodosum are also common features.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

In view of the fact that community-acquired pneumonia is not likely to be the primary diagnosis and that the patient is haemodynamically stable, antibiotics can be held off at present. A lymph node biopsy or fine-needle aspiration should be scheduled. Sputum samples should be sent for culture to identify the presence of acid-fast bacilli.



A computed tomography (CT) scan of the chest, abdomen and pelvis is also likely to be required. If the patient is having large volumes of haemoptysis, she should be kept in hospital for observation and her blood group should be assessed to allow a transfusion if required. If the haemoptysis is small volumes of blood-stained sputum then she can have further investigations as an outpatient.

CASE PROGRESSION

The patient coughed up 10 mL frank blood in the emergency department and was admitted under the medical team for further care. A CT scan of her chest, abdomen and pelvis showed hilar and mediastinal lymphadenopathy, as well as pleural thickening with two cavitating lesions in the right upper lobe. Ground glass changes were seen bilaterally. The abdomen and pelvis were reported to be normal.

A cervical lymph node biopsy was performed. The patient developed worsening dyspnoea, requiring oxygen therapy. A repeat chest x-ray showed bilateral pulmonary infiltrates. Sputum samples identified no organisms, with no acid-fast bacilli. Broad-spectrum antibiotics were commenced and the respiratory team was contacted to determine whether anti-tuberculosis treatment should be commenced at this stage.

The patient deteriorated significantly over the next 24 hours, requiring transfer to the intensive treatment unit for management of acute respiratory distress syndrome. The lymph node biopsy did not identify any organisms. A fine-needle aspiration of a cervical lymph node was performed in the intensive treatment unit and anti-tuberculosis treatment was commenced. The patient deteriorated further and was intubated and ventilated.

The second histological sample did not identify any organisms. Repeat sets of blood cultures yielded no growth and bronchial washings did not identify a causative agent. The patient continued anti-tuberculosis treatment and a repeat CT scan of the chest, abdomen and pelvis was performed, showing lung appearances consistent with acute respiratory distress syndrome and bilateral adrenomegaly. When the initial CT scan was re-reviewed, the adrenomegaly could be seen, although it was not highlighted at the time. An ultrasound-guided fine-needle aspiration of the adrenal gland was performed. This revealed the presence of fungal organisms, which were identified as *Histoplasma capsulatum*.

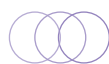
Final diagnosis: Histoplasmosis.

OUTCOME

The patient was treated with methylprednisolone, fludrocortisone (a mineralocorticoid) and amphotericin B. She had a protracted stay on the intensive treatment unit, developing several ventilator-associated pneumonias and renal impairment. She required intensive rehabilitation prior to returning home.

CASE DISCUSSION

Histoplasmosis is an infection of the fungal pathogen, *Histoplasma capsulatum*, which is endemic in North and Central America, and parts of Asia, Africa and South America. The



organism is present in acidic soil, particularly in areas inhabited by bats or around chicken coops, or riverbanks and mining regions. Most infected people remain asymptomatic throughout their lives, although in those that become unwell, the disease may present with acute pneumonitis that progresses to severe disseminated disease, or chronic histoplasmosis with cavitating lung lesions. Adrenal involvement is common, and CT appearances show central hypodensity of the adrenal glands, in keeping with both tuberculosis and histoplasmosis. Treatment involves antifungal agents, corticosteroids and possibly mineralocorticoids, depending on the extent of adrenal disease.

With thanks to Dr Thomas Simpson for his assistance with the case.

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CASE 98: HEADACHE AT THE CATTLE FARM

PATIENT HISTORY

A 29-year-old man presented to the emergency department complaining of fever and headache. He had become unwell 48 hours earlier, with symptoms of nausea, vomiting and widespread myalgia. He had been in South Sudan for the past fortnight, returning to the United Kingdom earlier that day (he came from the airport directly to hospital). He had been staying on his uncle's cattle farm in South Sudan. He had not noted any insect bites and had taken anti-malarial prophylaxis throughout his holiday. His partner accompanied him to South Sudan and had been well throughout the trip. The patient was born in South Sudan and had lived there until he was 12 years of age, when he came to live in the United Kingdom. He had no significant past medical history and took no regular medications aside from the current course of anti-malarial drugs. He worked as a journalist.

EXAMINATION

Initial observations: T 39.3°C, HR 100 bpm, BP 120/80 mm Hg, RR 20, SpO₂ 100% on room air.

The patient appeared unwell, intermittently drowsy and clinically dehydrated. His jugular venous pressure (JVP) was not visible and his lips were cracked. Respiratory and abdominal examinations were unremarkable. The patient was objectively photophobic and had mild neck stiffness. There was no obvious rash and no lymphadenopathy present.

INITIAL RESULTS

Routine blood results: WCC 8.4, Hb 150, Plt 316, Na 133, K 4.5, Creat 70, CRP 48.

Chest x-ray: clear lung fields.

DIFFERENTIAL DIAGNOSES

The patient has signs of meningitis and will need to be treated urgently for this. Bacterial and viral causes of meningitis should be suspected and investigated accordingly.

Cerebral malaria in adults presents with fever, headache, myalgia and drowsiness. Encephalopathy and seizures may develop. Anaemia and thrombocytopenia are common findings in malaria, neither of which this patient has.

Tuberculous meningitis should be suspected, particularly if the patient has any history of or risk factors for immunosuppression. The onset of this disease typically progresses over days or weeks rather than acutely, as in this case.



HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

Treatment for bacterial and viral meningitis should be commenced immediately. An appropriate regime would be intravenous ceftriaxone and aciclovir. A computed tomography (CT) scan of the brain should be performed to look for intracranial pathology and signs of elevated intracranial pressure (ICP). Depending on the CT results, a lumbar puncture should be performed, with the cerebrospinal fluid (CSF) being sent for bacterial and viral investigations.

An HIV test should be sent, along with three blood films to look for malaria parasites. Blood cultures should be taken. The infectious diseases team should be contacted to discuss further investigations based on the patient's travel history.

CASE PROGRESSION

The patient underwent a CT scan of the brain, which was unremarkable. He was treated with ceftriaxone and aciclovir for presumed meningitis. A lumbar puncture was performed, showing a raised leucocyte count (80% polymorphs, 20% lymphocytes) and a markedly elevated protein count of 3.7 g/L (reference range 0–0.44 g/L). No organisms were detected on the Gram stain. An HIV test was negative and no malaria parasites were seen on serial blood films.

A magnetic resonance imaging (MRI) scan was scheduled, but 48 hours after admission, the patient became increasingly drowsy and was failing to maintain his airway. He was taken to the intensive care unit where he was intubated and mechanically ventilated. At this point, a faint maculopapular rash was noted over his shins. CSF virology testing did not identify a causative agent. A repeat CT head scan showed no changes. Over subsequent days, numerous investigations were performed, and serology was sent for a panel of infectious diseases, including *Borrelia* and *Brucella* infections.

The infectious diseases team reviewed the patient and commenced doxycycline therapy for possible *Borrelia* meningitis or rickettsial (spotted fever) meningitis. Over the next 2–3 days, the patient became more alert and was able to protect his airway. He was extubated and transferred to a medical ward. Serological testing subsequently came back positive for *Rickettsia conorii*.

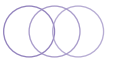
Final diagnosis: Rickettsial meningitis.

OUTCOME

The patient completed a course of doxycycline therapy and made a full recovery.

CASE DISCUSSION

Mediterranean spotted fever (also known as Boutonneuse fever) is a bacterial infection transmitted by dog ticks. The infection is endemic in the Mediterranean basin, central Asia



and throughout Africa. It is likely that the patient was bitten during his time on the farm. Patients classically present with fever, headache, maculopapular rash and a dark eschar at the site of the tick bite. Tetracyclines are the first-line antibiotics used to treat Mediterranean spotted fever.

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CASE 99: A PREGNANT WOMAN WITH LOSS OF VISION

PATIENT HISTORY

A 36-year-old woman presented to the emergency department complaining of a transient episode of blurred vision. She was 37 weeks pregnant. She had no previous episodes of visual impairment. She denied recent headaches or fevers. There was no pain in or around the eyes. She had experienced an uncomplicated pregnancy, although her blood pressure had been mildly elevated at 132/84 mm Hg at her last antenatal appointment. This was her first pregnancy. She had no past medical history and took no regular medications. She lived alone and worked as a graphic designer. She had never smoked and did not drink alcohol.

EXAMINATION

Initial observations: T 37°C, HR 80 bpm, BP 178/100 mm Hg, RR 22, SpO₂ 97% on room air.

The patient was distressed, although appeared otherwise well. She was tachypnoeic but her chest was clear to auscultation. Her calves were soft and non-tender. There was pitting oedema to mid-shin, which the patient reported to be a new finding. Her pupils were equal and reactive to light, visual fields were normal. Fundoscopy was reported to be unremarkable. The rest of the neurological examination was normal, with no increased tone, hyperreflexia or clonus present.

INITIAL RESULTS

Routine blood tests: WCC 4.6, Hb 108, MCV 84, Plt 265, Na 134, K 4.4, Creat 40, CRP 12.

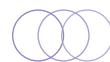
Urine dip: 2+ protein.

DIFFERENTIAL DIAGNOSES

The patient meets the criteria for pre-eclampsia: new-onset hypertension (SBP ≥ 140 mm Hg/DBP ≥ 90 mm Hg on two readings, or SBP ≥ 160 mm Hg/DBP 110 mm Hg on a single reading) with new-onset proteinuria after 20 weeks' gestation. Patients with pre-eclampsia may develop hypertensive retinopathy, resulting in spasm of the retinal arterioles and retinal haemorrhages.

The patient may have experienced an ischaemic or haemorrhagic stroke affecting the occipital cortex as a result of accelerated hypertension. Cortical blindness (often in association with posterior reversible encephalopathy syndrome [PRES]) associated with pre-eclampsia is a phenomenon where vasospasm or localised vasogenic oedema development, resulting in loss of vision, often bilaterally, that is typically reversible.

Serous retinal detachment is an uncommon cause of visual disturbance in patients with pre-eclampsia or eclampsia following the development of subretinal fluid accumulation.



HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The definitive treatment for pre-eclampsia and eclampsia is to deliver the fetus. This patient is 37 weeks' pregnant and the baby is likely to be mature enough to tolerate delivery without requiring corticosteroids to promote lung development.

The patient should be managed in a high dependency unit setting. Her blood pressure will need to be carefully controlled to minimise the risk to the mother while ensuring adequate placental flow. A typical blood pressure target is 140/90 mm Hg, but this will vary depending on individual patients. Labetalol, either administered orally or titrated as intravenous boluses +/- infusion, is typically the first-line anti-hypertensive in severe pre-eclampsia or eclampsia.

CASE PROGRESSION

The patient was managed on a specialist obstetric high dependency unit. Her hypertension responded to labetalol therapy and labour was induced. The patient delivered a healthy baby with no immediate complications. Immediately following delivery, the patient's blood pressure was found to have risen to 162/98 mm Hg. Soon after labetalol was administered, the patient complained of sudden loss of vision. She was examined and was found to have bilateral retinal detachments with reductions in visual acuity.

Final diagnosis: Retinal detachment secondary to pre-eclampsia.

OUTCOME

The patient gradually became normotensive and was weaned from labetalol over the next few days. She felt that her vision was improving at the time of discharge. Three weeks later, her retinal detachments had resolved and her visual acuity had returned to baseline.

CASE DISCUSSION

Retinal detachment in the context of pre-eclampsia arises when the neurosensory retina separates from the pigmented retinal epithelium and patients develop sudden loss of vision, often bilaterally. Patients typically regain their baseline visual acuity unless necrosis of the pigmented retinal epithelium has occurred.

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CASE 100: AN UNSOLVED MYSTERY

PATIENT HISTORY

A 23-year-old woman presented to hospital complaining of dyspnoea and left-sided chest pain that was worse on deep inspiration. She said that her symptoms had developed gradually over the preceding 24 hours, although she often had a dull ache or sense of 'fullness' on the left side of her abdomen and chest. She lived in China and had travelled to the United Kingdom for a holiday with her friend. She denied any past medical history and took no regular, herbal, or over-the-counter medications. She had never smoked and did not drink alcohol. She worked as a beauty therapist in a health spa and had no additional travel history.

EXAMINATION

Initial observations: T 37.6°C, HR 100 bpm, BP 108/60 mm Hg, RR 18, SpO₂ 98% on room air.

The patient appeared clinically well. She was of petite build and appeared underweight with an estimated body mass index (BMI) of 17–18. She was warm and well perfused. Her chest was clear to auscultation and heart sounds were normal. She complained of discomfort on palpation of the left upper quadrant.

INITIAL RESULTS

Routine blood tests: WCC 8.6, N^o 5.2, L^o 2.7, Hb 100, MCV 80, Plt 240, Na 139, K 4.2, Creat 45, CRP 7, Bili 8, ALT 12, ALP 26.

Additional bloods: D-dimer 4.4.

Chest x-ray: clear lung fields.

CASE PROGRESSION (1)

The patient was admitted under the medical team for management of a presumed pulmonary embolus, possibly due to immobility during the recent long-haul flight. The initial plan was for a ventilation/perfusion (V/Q) scan to identify potential pulmonary emboli. She was re-examined by the medical registrar who noted a mass in the right iliac fossa, which was subsequently thought to be her spleen.

After discussion with the radiology team, explaining that a pulmonary embolus may be present in the context of a possible malignant process, a computed tomography (CT) scan of the chest, abdomen and pelvis with views targeted at the pulmonary arteries was performed. This showed no enlarged mediastinal, hilar or axillary lymph nodes and no suspicious parenchymal lung lesions. The spleen was markedly enlarged measuring 19 × 12 cm in largest axial dimension and 27 cm in maximal cranio-caudally, and was infiltrated by multiple low attenuation rounded lesions of different sizes (see [Figure 100.1](#)). There were also multiple calcific foci. The spleen was displacing the transverse colon inferiorly and the stomach to the right. There was an impression of a mass lesion within the gastric body.

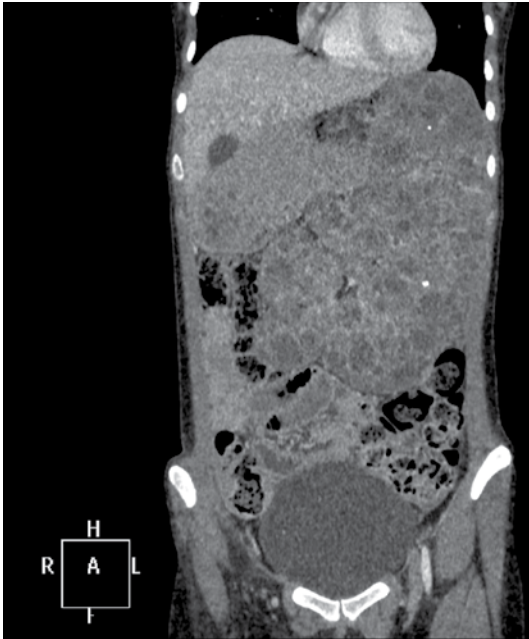
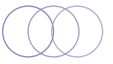


Figure 100.1 CT scan showing massive splenomegaly.

DIFFERENTIAL DIAGNOSES

The patient presents with massive splenomegaly, which is defined as a spleen measuring >20 cm. There are a limited number of causes of massive splenomegaly. In this case, lymphoma is probably the most likely diagnosis based on the patient's age, although there was no obvious lymphadenopathy seen on the CT scan.

Chronic myeloid leukaemia tends to affect people over the age of 50 years and patients will often have a prominent leucocytosis and may develop hepatomegaly alongside splenomegaly. Similarly, primary myelofibrosis tends to occur in older adults and patients have abnormal blood counts, with a typical blood film showing leucoerythroblastosis with poikilocytosis (teardrop-shaped red cells).

The patient may have a mild form of beta-thalassaemia intermedia, remaining asymptomatic until this point. It is very unlikely that she has undiagnosed beta-thalassaemia major.

Gaucher disease is a lysosomal-storage disorder that presents with anaemia, thrombocytopenia and hepatomegaly. Mild forms of this inherited disorder may present in adulthood.

Infectious diseases, particularly leishmaniasis, schistosomiasis and malaria, may also present with massive splenomegaly. This patient has only ever visited China (she lived in a major city and had not spent time in rural areas) and London.

HOW WOULD YOU MANAGE THIS PATIENT ACUTELY?

The patient should be assessed by the haematology team who may wish to perform a bone marrow aspiration or order alternative investigations to assess for lymphoma or



leukaemia. An endoscopy should be performed to arrange a biopsy of the possible mass lesion visualised within the gastric body – this may represent lymphoma. Depending on the initial investigations, the case may need to be discussed with the interventional radiology team to establish whether it is possible to safely perform a splenic biopsy to assess the low-attenuating lesions.

CASE PROGRESSION (2)

Following targeted questioning, the patient explained that she had been diagnosed with an enlarged spleen 5 years earlier at a routine medical assessment undertaken for employment purposes. She said that she had several tests at the time and was told that there was no need for concern and further investigation was not needed. She had remained well since, although she had unintentionally lost 5 kg in the past year and felt a constant sensation of fullness in the left upper quadrant.

Echinococcus, *Brucella*, schistosomiasis and leishmaniasis serology tests were negative, as were repeat malarial films. HIV, cytomegalovirus (CMV) and Epstein–Barr virus (EBV) IgM serology tests were negative. A G6PD test was negative. No acid-fast bacilli were seen on tuberculosis blood cultures. Protein electrophoresis did not identify a paraprotein band.

An oesophago-gastro-duodenoscopy (OGD) was performed, but no mass lesion was identified within the gastric body. Random biopsies of gastric and duodenal tissue showed no malignant features. A CT positron emission tomography (PET) scan was performed to identify possible lymph nodes that would be appropriate for biopsy, but none were seen. There were several small pelvic nodes with marginally increased uptake, likely to represent reactive nodes.

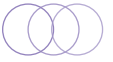
The interventional radiology team was approached to discuss whether a splenic biopsy would be possible. They advised an ultrasound scan to determine the nature of the low attenuation lesions initially. The ultrasound scan showed that the lesions were anechoic and some contained thin septations, which appeared avascular. The largest measured 3.2×2.4 cm. The interventional radiology team felt that biopsy would not be appropriate given the associated risks of haemorrhage.

The haematology team reviewed the patient and reported that the findings were possibly in keeping with splenic marginal zone lymphoma. A bone marrow biopsy found no evidence of marrow involvement by lymphoma, leishmaniasis or amyloidosis. Immunocytochemistry showed normal numbers of interstitial B and T lymphocytes and plasma cells.

Final diagnosis: Massive splenomegaly of unknown cause.

OUTCOME

No diagnosis was reached. The patient flew home to China with the results of the above assessments, where she planned to undergo further investigations.



CASE DISCUSSION

Unfortunately no diagnosis was reached in this interesting and highly unusual case. The team felt that they had excluded lymphoma and haematological malignancies but were unclear whether the cystic lesions represented metastatic deposits. They were reassured that the patient reported splenomegaly for at least 5 years, suggesting that the underlying pathology is chronic. The patient did not contact the UK team again so no further information is available at this point.

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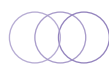
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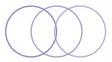
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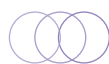
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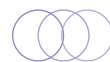
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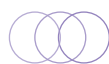
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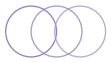
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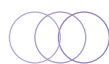
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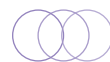
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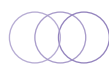
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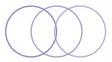
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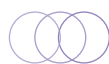
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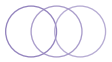
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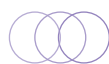
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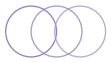
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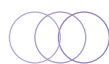
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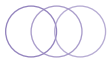
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